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ALCOHOLIC INTOXICATION

ITS DIAGNOSIS AND MEDICOLEGAL IMPLICATIONS

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BOSTON

The increasing popularity of high speed automobiles during the past decade has raised the problem of alcoholism above the level of morality and made it an issue of life and death. In 1936 motor vehicle deaths totaled 37,800. There were also 1,300,000 nonfatal traffic injuries, about 100,000 of them representing disabilities of a permanent character. In addition there were nearly 6,000,000 "property damage only" accidents. The total economic loss due to motor vehicle accidents for 1936 is conservatively estimated as $1,640,000,000. All summaries now available on fatal accidents show, on the average, that 7 per cent of the drivers and 11 per cent of the pedestrians "had been drinking" or were intoxicated.[1] In spite of the importance of establishing responsibility in accidents involving individuals who have been imbibing alcoholic beverages, the physician and the law still quibble about what constitutes alcoholic intoxication and what criteria are acceptable for establishing such a diagnosis.

Can it be established by scientific means (*a*) that an individual has imbibed alcohol and (*b*) whether or not that individual has become sufficiently intoxicated to impair the rational and full exercise of his mental and physical faculties?

There are so many simple methods of determining alcohol content in body fluid[2] that this aspect of the problem can no longer be considered impracticable. The body fluid which will give the most accurate estimation of the degree of alcoholism at the time the sample is obtained has been the subject of controversy.

Gettler and Freireich,[3] working on spinal fluid for the determination of alcoholic intoxication during life, elaborated the spinal fluid-brain ratio. In their opinion all persons having 0.265 per cent or more alcohol in the spinal fluid (or a spinal fluid-brain ratio below 1.4) are intoxicated. Alcohol enters the spinal fluid by diffusion from the blood[4] and leaves it by diffusion back into the blood once the blood alcohol level falls below that in the spinal fluid.[5] The alcoholic content of the spinal fluid in the lumbar sac rises more slowly than that in the blood, attaining its maximum two to three hours later.[6] The alcohol content in the cistern fluid, on the other hand, rises more promptly and closely approximates that of the blood. Cistern fluid would seem, therefore, the ideal fluid for the estimation of alcohol content of the brain in living persons. Since cistern puncture is at present a major medical procedure, it is not practical for the purpose of routine spinal fluid analyses for the determination of alcoholic intoxication.

The alcohol content of expired air is said to follow closely that of the blood. However, false values will be derived if a person has had a drink of alcoholic beverage within fifteen minutes before the sample of expired air is obtained, or if he regurgitates from the stomach.[7] Smith and Stewart[8] state that if expiration is complete a larger amount of alveolar air with a relatively higher alcohol content is obtained than if breathing is shallow.

Abels[9] reports that the alcohol content of saliva agrees with the blood alcohol within 3 per cent. But it has been found that the rate of increase of salivary alcohol in some instances exceeds the rate of increase in the blood and, furthermore, saliva contains a variable amount of oxidizable material equivalent in some cases to about 12 mg. of alcohol.[10]

The correlation between urinary alcohol concentration and the clinical manifestations of alcoholism is humorously portrayed in the accompanying illustration. Urinary alcohol may represent the degree of alcohol saturation at some preceding time rather than at the moment the sample is taken if the urine has been held in the bladder for some time before being voided.[11] If the urine is collected during the period of alcohol absorption, while the blood alcohol is rising, the urinary alcohol will be lower than the blood alcohol. Also if

This is one of a series of papers from the Advisory Committee on the study of alcoholism at the Boston City Hospital sponsored by the Works Progress Administration.

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6. Newman, H. W., and Mehrtens, H. G.: Reliability of Spinal Fluid Analyses in Diagnoses of Drunkenness, Proc. Soc. Exper. Biol. & Med. **30:** 725-727 (March) 1933. Mehrtens and Newman.[4]

7. Bogan, Emil: Drunkenness: Quantitative Study of Acute Alcoholic Intoxication, Am. J. M. Sc. **176:** 153-167 (Aug.) 1928.

8. Smith, Sydney, and Stewart, C. P.: Diagnosis of Drunkenness from Excretion of Alcohol, Brit. M. J. **1:** 87-90 (Jan. 16) 1932.

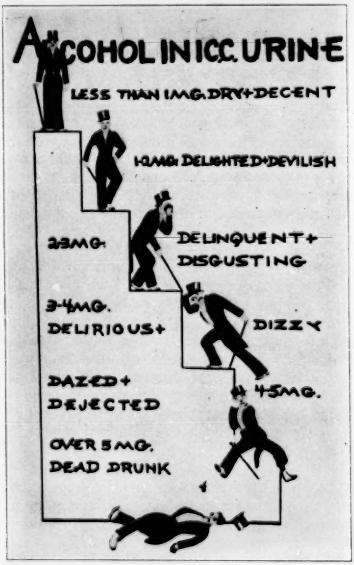
9. Abels, J. C.: Determination of Ethyl Alcohol in Saliva, Proc. Soc. Exper. Biol. & Med. **34:** 304-305 (May) 1936.

10. Friedemann, T. E.: Excretion of Ethyl Alcohol in Saliva and a Rapid Method for Its Determination, J. Biol. Chem. **105:** xxviii-xxix (May) 1934.

11. Hall, W. W.: Drunkenness: Naval Medicolegal Aspects of Its Diagnosis, U. S. Nav. M. Bull. **34:** 149-163 (April) 1936.

the urine is collected during the period of decline of blood alcohol the urinary alcohol will be higher than the blood alcohol.[8]

The blood alcohol concentration always represents the degree of alcohol saturation at the moment the blood sample is obtained. Though venous blood never actually reaches the peak of alcohol saturation that is attained in arterial blood, a rise or fall in the level of venous blood alcohol reflects a similar though greater rise or fall in the arterial level.[12] A venous blood alcohol determination done on a sample of blood taken within ninety minutes after ingestion of alcohol would be lower than the arterial blood alcohol concentration. After ninety minutes the two approximate each other,



Humorous portrayal of correlation between clinical manifestations of alcohol and urinary alcoholic levels. (From a sketch drawn by Mrs. Merrill Moore and reproduced with her permission.)

for thereafter equilibration of alcohol between arterial and venous blood and body tissues has taken place.[12] Blood appears to be a medium for analysis offering the best opportunity for giving the alcoholic suspect as fair an appraisal of his degree of alcoholism as is possible, in that (*a*) the amount of "nonalcoholic" oxidizable material in blood is negligibly small, (*b*) the blood alcohol concentration always reflects the degree of alcohol saturation at the moment the blood sample is obtained, (*c*) unlike other body fluids blood is always available and (*d*) its extraction does not necessitate the active participation of the subject.

It is becoming more and more obvious that drunkenness is no longer to be considered synonymous with alcoholic intoxication. Though alcoholic intoxication is an inseparable component of drunkenness when the latter exists, it is to be considered, rather, in a biologic sense. Heise [13] states that an excess of ethyl alcohol in the body fluids or tissues over the normal body alcohol,[14] even in the absence of gross manifestations of alcoholism, is to be considered alcoholic intoxication. It is known that small amounts of alcohol are capable of causing considerable disturbance with those activities requiring rapid integration and accurate coordination—without producing any gross signs that might lead even a competent observer to suspect drunkenness. As automobile driving, for example, is a common activity demanding at all times a high degree of rapid integration and accurate coordination, it becomes obvious how necessary and important it is to improve the criteria ordinarily employed in the determination of alcoholic intoxication.

Naville [15] found that slight intoxication in human beings starts when the blood alcohol content ranges from 0.1 to 0.2 per cent (from 100 to 200 mg. per hundred cubic centimeters of blood). Carlson,[16] working with 150 subjects, male and female, habitués and abstainers, concluded that none of his subjects showed sufficient intoxication to cause that degree of impairment which would cause him to be a menace to the public until the blood alcohol concentration exceeded 0.1 per cent. Turner [17] concluded that in general intoxication is not noticeable in the human being until the blood alcohol concentration is greater than 0.2 per cent. Using the method of blood alcohol determination described by Turner [18] based on the Naville modification of the Nicloux method, results similar to Turner's were obtained (shown in the accompanying table).[19]

From a group of fifty unselected cases admitted to the alcoholic ward of the Fifth Medical Service of the Boston City Hospital, the following general conclusions were drawn: Except for an odor of alcohol on the breath, clinical manifestations of intoxication do not appear until the blood alcohol exceeds 0.2 per cent; when the content is from 0.2 to 0.3 per cent, evidence of intoxication was definite and characterized chiefly by a change in affect, the patients being loquacious, crafty, witty, silly or belligerent, with some disturbance in locomotion; when it was from 0.3 to 0.4 per cent, walking was very unsteady or impossible, speech was thick, and drowsiness was the rule; when it was from 0.4 to 0.5 per cent there was no voluntary activity whatever, deep stupor supervening from which the patient could be roused by painful stimuli; when it was above 0.5 per cent practically all patients were in alcoholic coma. There was considerable overlapping in all the groups.

SUBCLINICAL INTOXICATION IN THE BIOLOGIC SENSE

What is most important from the medicolegal aspect is elucidation of subclinical intoxication or alcoholic intoxication in the biologic sense without any gross manifestations of drunkenness. Are there suffi-

12. Haggard, H. W., and Greenberg, L. A.: Studies in the Absorption, Distribution and Elimination of Ethyl Alcohol; Excretion of Alcohol in Urine and Expired Air and the Distribution of Alcohol Between Air and Water, Blood and Urine, J. Pharmacol. & Exper. Therap. **52**: 150-167 (Oct.) 1934.

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16. Carlson, A. J.: Criteria of Acute Alcohol Intoxication, Science **80**: 546 (Dec. 14) 1934.

17. Turner, R. G.: Blood Alcohol and Its Relation to Intoxication in Man, Proc. Soc. Exper. Biol. & Med. **32**: 1548-1552 (June) 1935.

18. Turner, R. G.: Blood Alcohol and Its Relation to Intoxication, J. Pharmacol. & Exper. Therap. **44**: 305-324 (March) 1932.

19. Data collected by Sydney Selesnick and Leon J. Kohinson during the course of a study on alcoholism at the Boston City Hospital.

cient scientific data available to prove beyond any reasonable doubt that such an intoxicated person driving an automobile is a potential public menace?

In what might be considered a crucial experiment Heise [19] gave to selected persons 150 cc. of whisky (equivalent approximately to two or three ordinary whiskies) and then put them into automobiles to observe their reactions while driving. He noted a definite variation from the normal in acts involving the avoidance of obstacles placed on the road and in backing the car. Reaction time between a given signal and the application of brakes was increased. All the subjects showed lack of appreciation of changes in judgment and motor control. Yet, without exception, every one was able to pass creditably the ordinary tests used to determine drunkenness and to perform the routine acts involved in driving. Heise says that it is not the drunk who constitutes the menace in driving but the drinking driver. He believes that loss of efficiency and judgment occurs even with blood alcohol concentrations as low as 0.02 per cent (20 mg. per hundred cubic centimeters of blood).

Bahnsen and Vedel-Petersen,[20] in an extensive and painstaking group of studies on a large number of subjects, including both habitués and abstainers, tested for speed reaction, speed of muscular contraction, muscle coordination and ability of concentration before and after the ingestion of given amounts of alcohol. Even the progress of practice that follows several repetitions of the same experiment was checked and controlled. The results of the study show that not only does alcohol retard all the observed reactions and tend to lower the final grade of their performance but it also nullifies the progress of practice. It is important to note that, though not one of their large group of subjects was described as clinically intoxicated in any sense, their performances were inferior. Analyzing the results of Bahnsen and Vedel-Petersen on the basis of the blood alcohol concentrations, Schmidt [21] shows that the maximum effects of the alcohol take place just after the maximal blood alcohol concentration is attained, which occurs from fifteen to ninety minutes after ingestion of the alcoholic beverage.

Cattell [22] feels that it is fairly well established by his experiments that a dose of 20 Gm. of alcohol (equivalent to slightly more than 2 ounces [60 cc.] of whisky) lowers the intelligence quotient and diminishes the power of recalling past experiences. In a comprehensive study on a group of six men including habitués and abstainers, Hollingworth [23] concludes that in all the mental and motor tests used by him the effect of alcohol is to reduce the score. In all cases the effect varied directly with the size of the dose. It has been demonstrated [24] that one glass of beer increased the incidence of error in a simple experiment (precision in making a number of dots) by 21 per cent; peripheral vision (which catches moving objects) may be affected up to 11 per cent. After an amount of alcohol equivalent to 2¼ ounces (67.5 cc.) of whisky errors in typewriting increased 40 per cent for the next two hours and after twice this quantity of alcohol by 70 per cent; alcohol in small or moderate amounts has been shown to impair coordination of leg movements; the speed with which the gaze is directed to fresh objects is measurably impaired by the drinking of alcohol.[25] Newman [26] gave alcohol intravenously to nine patients. The average maximum attained by the alcohol in the blood stream was 112 mg. per hundred cubic centimeters (0.112 per cent). A third of them evidenced a feeling of well being which verged on euphoria. All showed an increased loquacity. Many had slight slurring of speech. Although drowsiness was present in most cases to some degree, there was no evidence of loss of contact with reality.

Schwarz,[27] in a discussion of the quantitative determination of the alcohol content of the blood and its significance in connection with automobile accidents, evaluates the results of alcohol analyses in more than 1,000 cases. He concludes that his results dispel any doubt as to the practical value of the quantitative alcohol analysis. Concentrations between 0.1 and 0.15 per cent were accompanied by signs of alcoholic intoxication in 93.7 per cent of cases. The latter concentrations were found most frequently in instances of traffic accidents. Excessive speed and neglect of safety rules, as the result of the excitation caused by the alcohol, were the usual causes of such accidents. With the

TABLE 1.—*Correlation Between Blood Alcohol Levels and Clinical Manifestations of Alcoholism* *

		Blood Alcohol in Gm./100 Cc.				
		Under				Over
Clinical Manifestations of Alcoholism	Cases	0.2	0.2-0.3	0.3-0.4	0.4-0.5	0.5
Odor of alcohol; no other signs	5	5	0	0	0	0
Odor of alcohol with change in affect	12	0	4	4	4	0
Thick speech; unable to walk; drowsy	15	0	1	8	6	0
Stupor rousable by painful stimuli	13	0	0	0	9	4
Coma	5	0	0	0	0	5

* The method of blood alcohol determination described by Turner based on the Naville modification of the Nicloux method was used.

content of blood alcohol above 0.20 per cent, Schwarz thinks it may be asserted that the individual in question is incapable of coping even with comparatively simple traffic problems.

The fact that some individuals are able to imbibe large quantities of alcohol without showing any apparent signs of intoxication has been a major argument against the acceptance of alcohol levels of body fluid as criteria for degrees of intoxication. Various reasons have been proposed for this difference in tolerance to alcohol, including decreased absorption from the gastrointestinal tract, increased elimination by the lungs and kidneys, increased tissue resistance to high concentrations of alcohol and increased oxidation of the alcohol by the tissues. In a recent review of the literature Newman [28] points out that the nature of alcohol tolerance is still a controversial subject. The older literature leaned toward increased oxidation of alcohol to explain it. Recent studies seem to prove this theory untenable.

COMMENT

At the request of the Minister of Transport the British Medical Association recently appointed a special committee to investigate and report on the relation between road accidents and alcoholism. The summary

20. Bahnsen, Paul, and Vedel-Petersen, K.: Alcohol Studies: Experiments on Drivers of Motor Vehicles, J. Indust. Hyg. **16:** 304-322 (Sept.) 1934.
21. Schmidt, Max (Copenhagen): Alcohol Studies: Concentration of Alcohol in Blood, J. Indust. Hyg. **16:** 353-365 (Nov.) 1934.
22. Cattell, R. B.: Effects of Alcohol and Caffeine on Intelligent and Associative Performance, Brit. J. M. Psychol. **10:** 20-33 (May) 1930.
23. Hollingworth, H. L.: Influence of Alcohol, J. Abnor. Psychol. **18:** 204-237 (Oct.-Dec.) 1923.
24. Efficiency on the Road: The Effect of Alcohol, Brit. M. J. **1:** 1280 (June 22) 1935.
25. The Relation of Alcohol to Road Accidents, Report by British Medical Association Committee, Brit. M. J. **1:** 57-59 (July 27) 1935.
26. Newman, H. W.: Alcohol Injected Intravenously: Some Psychological and Psychopathological Effects in Man, Am. J. Psychiat. **91:** 1343-1352 (May) 1935.
27. Schwarz, Fritz: Some Experiences in Quantitative Determination of Alcohol Content of Blood, Schweiz. med. Wchnschr. **67:** 54 (Jan. 16) 1937; abstr. J. A. M. A. **108:** 767 (Feb. 27) 1937.
28. Newman, H. W.: Recent Studies on Alcohol, Am. J. M. Sc. **192:** 868 (Dec.) 1936.

of the committee [28] in part is as follows: Alcohol in small or moderate amounts has been shown to diminish attention and control, to affect reasoning adversely, to affect adversely the power to make movements dependent on rapid and accurate coordination, and the ability of the eyes to follow clearly an object brought nearer and nearer. After taking alcohol the automobile driver may believe himself to be driving better but in fact his body works less efficiently. This happens even if alcohol is taken in moderate quantities some hours before driving and especially on an empty stomach.

In this country the American Medical Association, recognizing that "the street is a battlefield and that thousands of our citizens are killed and disabled by reckless, incompetent and physically disqualified individuals," has appointed a committee to study problems on motor vehicle accidents. The committee states in part in its preliminary report [29] "Since it is impossible to diagnose drunkenness adequately—drunkenness from symptoms alone—it is important that the chemical observation of the blood, urine, saliva or breath for alcohol be used to confirm obvious intoxication."

The drinking driver subclinically intoxicated is at the present time a distressing medicolegal problem. Given a clever attorney to protect his interests he all too frequently escapes conviction for driving under the influence of alcohol. Even competent members of the medical profession could not prove to the satisfaction of the court that such an individual was unfit to drive an automobile on clinical grounds alone. It has been adequately shown, however, that there are scientific means which deal out impartially data capable of including or excluding beyond any reasonable doubt the question of alcoholic intoxication. These means ought to be widely employed.

Repeated experiences have shown that, in accidents in which a person has been traumatized, drowsiness, stupor or coma cannot be safely attributed to alcoholism simply because there is an odor of alcohol on the breath. In such cases it is vital to exclude the possibility of cerebral concussion, brain laceration, fractured skull, extradural hemorrhage and subdural hematoma. In such cases blood alcohol determinations, especially if they show minimal degrees of alcohol in the body fluids, would cry out for the necessity of searching for some other factor as the cause of the drowsiness, stupor or coma.

Everard Dickson, British magistrate, asks "Are physicians positive that they can make an examination which will enable them to say beyond all reasonable doubt in all cases that the accused person is or is not to a serious extent affected by drink and that the real explanation of the symptoms exhibited is not to be found in some other condition?" [30] It can be determined by blood alcohol estimations whether or not an individual has an abnormal amount of alcohol in his body fluids and tissues. The adverse effect of abnormal amounts of alcohol in the body has been demonstrated. It has also been shown that the adverse effect of alcohol increases with greater concentrations of alcohol in the tissues. It remains simply to state that any individual who is under the influence of alcohol, however slight it may be, is unfit to assume the responsibilities associated with driving an automobile. The greater the degree of intoxication the greater the gravity of the offense, for the law does not recognize drunkenness as a defense, for a man intends the consequences of his own acts. The driving public must be impressed with the seriousness of even minor degrees of intoxication, the courts with the responsibility of the drinking driver. The Committee on the Driver of the National Safety Council has for the present accepted 0.150 per cent blood alcohol as the level above which alcoholic intoxication is definite.[29] This offers too wide a margin of laxity for the drinking driver. Experimental studies on habitués and abstainers show almost consistently that there occur appreciable disturbances in psychomotor activity at far lower levels of blood alcohol. It is likely that this level will be lowered in the future.

An objection may be raised relative to the privilege of the suspected alcoholic individual to refuse to submit to the extraction of blood. It is true that nobody by law can be made to testify against himself. Finger prints might similarly be categorized in that they too may be used as testimony against an individual, yet they are taken freely with the tacit approval of the law. With regard to blood extraction it can be pointed out that the same objections were raised regarding blood group tests in cases of disputed parentage. However, laws were enacted in New York State in 1935 authorizing the courts to order blood grouping tests in cases of disputed parentage and in civil suits when relevant to issues, and to receive the results in evidence. Shortly thereafter similar laws were enacted in Wisconsin and there are now bills pending before the legislatures of Montana, California and New Jersey.[31] Similar laws can be enacted with regard to extraction of blood for the estimation of the content of alcohol in the blood. Any infringement on civil rights exposes the offending individual to the curtailment of certain of his liberties by law. If the law will recognize the importance of blood alcohol determinations in accidents having medicolegal aspects, the offending individual will cease to have the liberty of refusing to allow the extraction of blood. The evidence to be obtained is just as likely to be favorable to the suspect as not.

SUMMARY

It is important to have definite criteria as a basis for the diagnosis of alcoholic intoxication in accidents involving individuals who have imbibed alcoholic beverages. The chemical determination of body fluid alcohol offers a scientific means of establishing whether or not an individual has imbibed alcohol and of estimating the degree of alcoholic intoxication. Blood as a medium for analysis is preferable to spinal fluid, urine, saliva and expired air, because it contains a negligibly small amount of nonalcoholic oxidizable material, its alcoholic content represents the degree of alcohol saturation at the moment the blood sample is obtained, it is always available, and its extraction does not necessitate the active participation of the subject. There are sufficient scientific data to prove that subclinical intoxication—or alcoholic intoxication in the biologic sense without any gross manifestations of drunkenness—can produce sufficient interference with psychomotor activity and neuromuscular coordination to render such an affected individual a potential public menace. Blood alcohol determinations can detect these degrees of alcoholic intoxication which ordinarily escape the detection of competent physicians. Criteria, therefore, must be established which include body fluid alcohol determinations as part of the diagnostic armamentarium.

29. Preliminary Report of the Committee to Study Problems of Motor Vehicle Accidents, J. A. M. A. **108**: 2137 (June 19) 1937.

30. Dickson, Everard: Medicolegal Aspects of Drunkenness, Med.-Leg & Criminol. Rev. **3**: 274-281 (Oct.) 1935.

31. Report of the Committee on Medicolegal Blood Grouping Tests, J. A. M. A. **108**: 2138 (June 19) 1937.

A RAPID CHEMICAL TEST FOR INTOXICATION EMPLOYING BREATH

A NEW REAGENT FOR ALCOHOL AND A PROCEDURE FOR ESTIMATING THE CONCENTRATION OF ALCOHOL IN THE BODY FROM THE RATIO OF ALCOHOL TO CARBON DIOXIDE IN THE BREATH

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Chemical tests for intoxication have been used very little in the United States in spite of the fact that certain of them were available more than twenty years ago and even though procedures employing blood and urine have been official for some time in certain European countries, notably Sweden, Switzerland and Germany. The adoption of such tests in this country appears to have been hindered by both legal and practical difficulties. First there is the question of whether our states can legally compel a person to give a specimen of blood or urine.[1] On the practical side there is frequently a long delay before a specimen of blood or urine can be obtained, and during this interval the subject's condition may materially change. With blood one must wait for the arrival of a physician or a properly trained technician. As to urine, we agree with Southgate and Carter [2] that intoxicated subjects frequently will not or cannot produce a specimen when asked to do so. Finally, none of the existing tests can be performed at the scene of the accident or in most local police stations, which means that the subject may be detained for hours or even days until the analyst's report is available. The procedure described in this paper was developed with the object of eliminating or minimizing these difficulties.

BODY MATERIALS SUITABLE FOR PREDICTING THE CONCENTRATION OF ALCOHOL IN THE BRAIN

The absorption of alcohol from the gastro-intestinal tract is rapid. Recent experiments in our laboratory [3] with fasting dogs which received 3 Gm. of alcohol per kilogram by stomach tube and were killed at various intervals showed an average absorption of 52.3 per cent in fifteen minutes and 99 per cent in three hours. This dose corresponds to a little more than a pint of whisky for a man weighing 150 pounds (68 Kg.). With smaller doses the speed of absorption was greater. Food in the alimentary tract somewhat delays absorption.[4]

After absorption alcohol is rapidly transported to all parts of the body, where it is stored in proportion to the water content of each body material.[3] The entire body thus reaches a condition of storage equilibrium as to alcohol, and as the total alcohol content decreases —mostly by oxidation—the concentration ratios of alcohol in the various body materials remain the same. After equilibrium occurs it is thus possible to estimate the distribution of alcohol all over the body from the concentration in any part. The brain, blood and liver reach equilibrium almost at once. The correlation between alcohol level in the blood and in the brain is shown in figure 1. These data show that with widely varying doses of alcohol and with test periods ranging all the way from fifteen minutes to twelve hours after the administration of alcohol, the concentration of alcohol in the brain could always be closely predicted from that in the blood. We found a similar parallelism between the alcohol level in the liver and in the brain. With muscle there was a lag for one or two hours, after which the concentration in the muscle too could be used to predict that in the brain. Even the alimentary tract and its contents were found to attain equilibrium within from two to three hours and could then be used for estimating the concentration of alcohol in the brain.

Simultaneous analyses for alcohol in the blood and in the lumbar spinal fluid made in forty-six consecutive cases at the Indianapolis City Hospital showed a close parallelism between the two as to alcohol

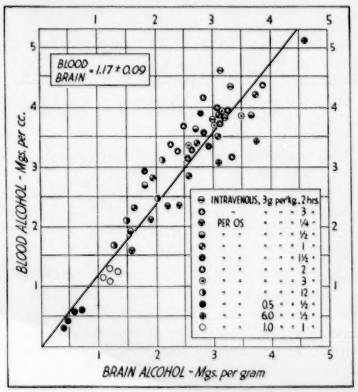

Fig. 1.—Correlation between the concentration of alcohol in the brain and in the blood in fifty-three dogs (from Harger, Hulpieu and Lamb [3]).

(fig. 2). Carlson and his associates [5] have shown a good correlation between the level of alcohol in the blood and in the urine (fig. 3). There is also a fixed relationship between the level in the saliva and in the blood, as pointed out by Linde.[6] Yant and Schrenk [7] have reported almost identical results regarding the distribution of methyl alcohol in various body tissues and fluids. Finally, breath may be employed for predicting the concentration of alcohol in the body. In 1910 Cushney [8] pointed out that the distribution between the alveolar air and the blood of such volatile substances as acetone, ether and alcohol obeys Henry's law, which means that the concentration of alcohol in the blood may be predicted from the concentration in the alveolar

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8. Cushny, A. R.: On the Exhalation of Drugs by the Lungs, J. Physiol. **40:** 17 (April 26) 1910.

air. Emil Bogen in 1927 [9] first proposed use of analysis of the breath as a test for intoxication. His pioneer work in this field included a comparison of the concentration of alcohol in the breath with that in the urine in fifty cases. A constant relationship between the amount of alcohol in the blood and in the alveolar air has been further confirmed by the work of Liljestrand

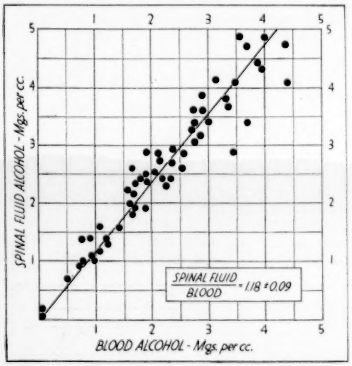

Fig. 2.—Correlation between the concentration of alcohol in the blood and in the spinal fluid in forty-six human subjects (from Harger, Hulpieu and Lamb).

and Linde [10] and that of Haggard and Greenberg.[11] It is thus evident that the concentration in the brain can be predicted from that in the blood, urine, spinal fluid, saliva and breath. The use of breath has appealed to us because breath may be obtained with less difficulty than any of the other substances mentioned.

THE RATIO OF ALCOHOL TO CARBON DIOXIDE IN THE BREATH AS A MEASURE OF THE ALCOHOL IN THE BLOOD

The carbon dioxide tension of pulmonary blood and alveolar air are practically identical, and in 1905 Fitzgerald and Haldane [12] reported that the alveolar air of normal subjects always contains close to 5.5 per cent of carbon dioxide by volume. Subsequent work by Higgins,[13] Turner [14] and Main [15] indicated some fluctuation due to posture, fasting and other factors, but this is not very great and most of it may be eliminated by placing the subject in a sitting or a reclining position. Since the tendency of carbon dioxide to escape from the blood and other body fluids is constant, it would seem that the quantity of alcohol which accompanies the carbon dioxide should vary directly with the concentration of alcohol in the blood. The carbon dioxide content of a sample of breath may be used as a measure of the fraction of alveolar air in such a sample. However, it is likely that some of the carbon dioxide in breath represents diffusion from bronchioles and bronchi, but alcohol probably diffuses also from these surfaces in much the same ratio as it does in the alveoli. In 1931 one of us [16] reported a satisfactory prediction of the concentration of alcohol in the blood from the ratio of alcohol to carbon dioxide in the breath. As to the distribution of alcohol between alveolar air and blood, Liljestrand and Linde,[10] using human subjects, found that 2,000 cc. of alveolar air contains the same quantity of alcohol as 1 cc. of blood. Haggard and Greenberg [11] reported that for dogs this ratio is 1:1,145. Bogen [9] stated that in the case of human subjects 2 liters of expired air contains slightly more alcohol than 1 cc. of urine. Our results with human subjects agree well with those of Liljestrand and Linde and we have adopted the ratio of 1:2,000 for alveolar air and blood. If alveolar air contains 5.5 per cent of carbon dioxide, the weight of carbon dioxide in 2 liters of such air at body temperature will be close to 190 mg. The weight of alcohol in 1 cc. of blood should therefore equal the quantity of alcohol in the breath which accompanies 190 mg. of carbon dioxide.

Use of the ratio of alcohol to carbon dioxide should eliminate errors due to fluctuations in the proportion of alveolar air in the sample of breath or, rather, fluctuations in the extent to which a given sample of breath has approached equilibrium relative to the alcohol content of the blood. Judging from its carbon dioxide content, we found that the proportion of alveolar air in 500 cc. of breath may vary from about 40 per cent to 100 per cent, depending on the extent to which the lungs were emptied and the length of time the air was held in the lungs. In addition, the use of the ratio of alcohol to carbon dioxide permits the test to be done by means of a pump which sucks the breath through the apparatus. This is particularly advantageous with subjects who will not or cannot blow into a breath

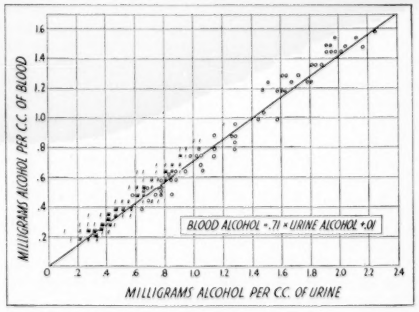

Fig. 3.—Correlation between the concentration of alcohol in the urine and in the blood (after Carlson and his associates).

container. In this case breath is mixed with some outside air, but, since air contains no alcohol and only 0.03 per cent of carbon dioxide, the ratio of alcohol to carbon dioxide in the breath may still be used for predicting the concentration of alcohol in the body.

REAGENT FOR ALCOHOL

As a result of rather extensive experiments, we have developed a reagent for alcohol the use of which

9. Bogen, Emil: Drunkenness: A Quantitative Study of Acute Alcoholic Intoxication, Am. J. M. Sc. **176**: 153 (Aug.) 1928, and J. A. M. A. **89**: 1508 (Oct. 29) 1927.

10. Liljestrand, G., and Linde, P.: Ueber die Ausscheidung des Alkohols mit der Exspirationsluft, Skandinav. Arch. f. Physiol. **60**: 273, 1930.

11. Haggard, H. W., and Greenberg, L. A.: Studies in the Absorption, Distribution and Elimination of Ethyl Alcohol: II. The Excretion of Alcohol in Urine and Expired Air and the Distribution of Alcohol Between Air and Water, Blood and Urine, J. Pharmacol. & Exper. Therap. **52**: 150 (Oct.) 1934.

12. Fitzgerald, M. P., and Haldane, J. S.: The Normal Alveolar Carbonic Acid Pressure in Man, J. Physiol. **32**: 486 (July 13) 1905.

13. Higgins, H. L.: The Influence of Food, Posture, and Other Factors on the Alveolar Carbon Dioxide Tension in Man, Am. J. Physiol. **34**: 114 (April 1) 1914.

14. Turner, A. H.: The Circulatory Minute Volumes of Healthy Young Women in Reclining, Sitting and Standing Positions, Am. J. Physiol. **80**: 601 (May) 1927.

15. Main, R. J.: Variations in Alveolar Carbon Dioxide in Man During Hunger, Am. J. Physiol. **119**: 7 (May) 1937.

16. Harger, R. N.: Science News, Science **73**: 10 (April 3) 1931.

involves a minimum of laboratory procedures. This reagent consists of a weak solution of potassium permanganate in the presence of approximately 55 per cent sulfuric acid by weight. When air or breath is passed through this solution any alcohol present will be absorbed and the absorbed alcohol will react rapidly and quantitatively with the permanganate. This reaction will take place at ordinary temperatures and does not require the application of heat. The change in color is a decisive one, which is marked by the disappearance of the initial purple and the formation of a very faint yellowish brown. In the high concentration of the sulfuric acid employed the reaction of the permanganate is different from that in the usual permanganate titration, in which the strength of sulfuric acid is rarely above 5 per cent. In the classic permanganate titration the manganese is reduced from a valence of seven to a valence of two. In our procedure the manganese is not reduced to a valence of two, and the faint yellowish brown solution which results is capable of further oxidation when properly diluted and heated with such substances as oxalic acid. Our reagent is not affected by acetone, which is of course of considerable importance in testing subjects suffering from ketosis. Experiments conducted with acetone alone and with solutions of alcohol containing ten times as much acetone as alcohol showed that the acetone in no way affected the behavior of the reagent. Other alcohols and ether will also reduce permanganate under the condition employed, but these substances would hardly be present in the body of an automobile driver, or, if they were present, they would be included in the substances which are banned by the driving laws of most states. The decisive change in color of the reagent may have a marked psychic effect on the subject being tested and has frequently enabled us to secure truthful statements from alcoholic subjects who at first denied drinking. The behavior of the reagent is easily demonstrated in court. The breath odors resulting from the consumption of onions, garlic, sen-sen and cloves do not affect the reagent, and tests conducted on more than 1,000 normal and hospitalized subjects failed to reveal the presence of any substance in the breath of these nonalcoholic people that was capable of reducing the permanganate reagent.

REAGENTS AND APPARATUS

Solution I is approximately sixteen normal sulfuric acid. It is prepared by slowly pouring three volumes of chemically pure concentrated sulfuric acid into four volumes of distilled water. When cool, the reagent is ready for use. It should be stored in a clean glass-stoppered bottle. Under no circumstances should it be allowed to come in contact with organic materials, such as rubber.[17]

Solution II is twentieth normal potassium permanganate solution, which is prepared by dissolving 1.58 Gm. of chemically pure potassium permanganate in enough water to make one liter. One should use a good grade of distilled water and glassware which has been cleaned first with soap and then with concentrated sulfuric acid containing some dissolved chromic acid and then washed well with distilled water. If stored in a dark place the solution will keep well for at least six months. The permanganate solution may be standardized against chemically pure sodium oxalate according to the directions given in works on quantitative analysis. However, we have found that solutions prepared according to the directions given assay very close to the desired strength.

A convenient form of apparatus is shown in figure 4.[18] The all glass reaction tube (*B*) carries an inlet tube extending to the bottom and ending in a perforated bulb. A funnel-shaped opening is provided at the top for the introduction of the solutions and is closed by means of a glass stopper. An etched line indicates a volume of 10 cc. A glass stopcock at the bottom permits drainage of used solutions. The upper end of the inlet tube is connected to a piece of small rubber tubing about 8 inches long (*A*).

In order to illuminate the lower end of tube *B*, the instrument board to which it is attached is provided

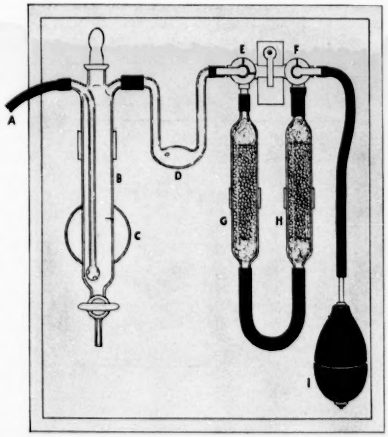

Fig. 4.—Apparatus for the simultaneous determination of alcohol and of carbon dioxide in the breath.

with a window of frosted glass (*C*), and a flashlight bulb with battery is placed behind this window. The outlet tube from *B* is connected to a glass trap (*D*) in order to prevent droplets of fluid from being carried over into the remaining parts of the apparatus. Trap *D* connects with a three way valve (*E*), which permits the gas to pass either to the dehydrating tube (*G*) or directly across to a second three way valve (*F*). The water-removing tube (*G*) is filled with Dehydrite. A piece of heavy-walled rubber tubing connects the lower end of tube *G* with the lower end of tube *H*. Tube *H* is filled with Ascarite for the absorption of carbon dioxide. The outlet from valve *F* is connected by means of rubber tubing to a rubber bulb (*I*), which is fitted with metal check valves so that it can be used as a suction pump. The three way metal valves (*E* and *F*) are arranged so as to leave tubes *G* and *H* out of the circuit or to send the gas stream successively through them.

When not in use, the Ascarite tube (*H*) is stored in a larger glass tube, which is closed by means of a paraffined cork and which contains a quantity of a

17. When 10 cc. of this acid is mixed with 1 cc. of solution II, the resulting purple fluid should undergo practically no change in color for at least one hour.

18. This apparatus, mounted in a small carrying case, may be obtained from the Medical Specialties Company of Indianapolis, which company has been licensed by the Indiana University Foundation under patents held by the foundation.

mixture of Ascarite and Dehydrite in order to keep its interior free from moisture and carbon dioxide. Under these conditions of storage the sealed-in Ascarite tubes (*H*) will retain their weight indefinitely. When tube *H* is not in position the open end of the rubber tube at the bottom of tube *G* should be closed by means of a glass or metal plug in order to prevent the entrance of moisture into tube *G*. In addition to the apparatus shown in figure 4 there should be provided a number of balloons, a glass adapter for connecting the inflated balloons to a short piece of rubber tubing, a screw clamp for closing the rubber tube, a short glass nipple for connecting with tube *A* and three circular brass rings for roughly measuring the volume of breath contained in the balloon. These brass rings have diameters of 156 mm., 124 mm. and 98.5 mm., respectively, and correspond to spheres with volumes of 2,000 cc., 1,000 cc. and 500 cc. When the device is being used as a pump to draw the breath stream directly through the apparatus, the inlet tube *A* is connected to a short length of rubber tubing to which

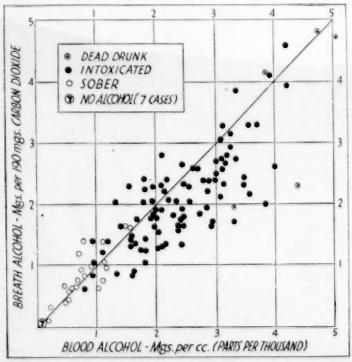
DEAD DRUNK
INTOXICATED
SOBER
NO ALCOHOL (7 CASES)
BREATH ALCOHOL - Mgs. per 100 mgs. CARBON DIOXIDE
BLOOD ALCOHOL - Mgs. per cc. (PARTS PER THOUSAND)

Fig. 5.—Correlation of the concentration of alcohol in the blood and in the breath in 121 human subjects.

are attached a few pieces of fine hair to show when this tube is held in the outgoing breath stream.

In addition to the apparatus described we suggest a bottle fitted with a rubber stopper with two holes, one carrying a glass inlet tube extending to the bottom of the bottle and the second a glass ell which ends just below the rubber stopper. When a weak solution of alcohol (about 0.5 per cent) is placed in the bottle and air is drawn through the solution it will serve as an "artificial drunk." This will permit the operator to familiarize himself with the end point of the reaction and also to demonstrate the reaction in court. A second bottle fitted up in the same way may be used for making qualitative tests for alcohol in the urine, since the urine of the alcoholic subject will serve as the fluid in the "artificial drunk."

PROCEDURE FOR TESTING SUBJECTS

Preliminary Test.—In this step tube *H* is not used and valves *E* and *F* are turned to shunt the gas past tube *G* and directly out by way of the rubber tube and bulb *I*. Place in the reaction tube (*B*) about 10 cc. of solution I, followed by exactly 1 cc. of solution II; replace the stopper and mix the contents of tube *B* by one or two strokes of the bulb pump. If the subject will cooperate, have him collect slightly more than 2 liters of breath in one of the balloons. Connect the balloon to a glass adapter and the other end of the adapter to a short piece of rubber tubing which is closed by a screw clamp. Release air from the balloon until it fits the large ring (2 liters). Without delay connect the rubber tube on the glass adapter to the inlet tube *A* by means of a small glass nipple. Open the pinch clamp and allow the breath to pass fairly rapidly through the apparatus but not fast enough to cause the liquid in tube *B* to foam over into trap *C*. If 2 liters of breath will not decolorize the solution in tube *B* the subject's blood contains less than 0.35 mg. of alcohol per cubic centimeter, if any, and he may be discharged with the report that he has not been drinking, at least to an appreciable extent.

If the purple color of the fluid is removed by less than 2 liters of breath, the quantity of breath used for the test is roughly measured by comparing the diameter of the balloon containing the remaining breath with the two smaller brass rings. If more than 1,000 cc. of breath has been used, the subject's blood contains less than 0.7 mg. of alcohol per cubic centimeter and he is probably not under the influence of alcohol. If the purple color is removed by less than 1,000 cc. of breath, one should perform the quantitative test described hereafter. The end point in the reaction is marked by the disappearance of the last trace of purple, which leaves a faint yellowish brown fluid.

If the subject will not or cannot cooperate, the short tube with some fine hairs attached is connected to tube *A* and its open end held about 1 inch from the subject's nose or mouth. The breath is then drawn through the apparatus by means of the pump. The action of the pump should be synchronized with the subject's respiration, and the intake stroke should coincide with an expiration. The fine hairs on the inlet tube will indicate when this tube is held in the breath stream. If fifty strokes of the pump are not sufficient to decolorize the reagent, the subject has probably not been drinking to any appreciable extent.

Quantitative Test.—This is performed exactly as the preliminary test except that tube *H* (previously weighed) is connected in position, as shown in figure 1, and valves *E* and *F* are turned so as to include tubes *G* and *H* in the path of the gas. Either the balloon or the pump may be used to collect the breath. When the test is finished, which is indicated when the last trace of purple has just disappeared from the fluid in tube *B*, tube *H* is at once replaced in its container and the container closed. Subsequently tube *H* is sent to a laboratory for weighing. When the balloon is used, the volume of breath passed through the aparatus may be accurately measured by disconnecting the rubber bulb and connecting the outlet tube to a gas buret filled with water.

CALCULATIONS

We have found that under the conditions employed 1 cc. of twentieth normal potassium permanganate solution is just decolorized by 0.175 mg. of ethyl alcohol. The weight of carbon dioxide absorbed by tube *H* tells how much alveolar air contained 0.175 mg. of alcohol. It is then a simple problem in proportion to calculate the quantity of alcohol which accompanied 190 mg. of carbon dioxide, that is, the weight of alcohol in 2 liters of alveolar air and therefore the weight of alcohol of 1 cc. of the subject's blood. Let x equal milligrams

of alcohol in 2 liters of alveolar air and w the increase in weight of tube H in milligrams. Then,

$$\frac{x}{190} = \frac{0.175}{w} \quad \text{Solving, } x = \frac{33.25}{w}$$

Thus, to calculate the milligrams of alcohol in 2 liters of alveolar air or in 1 cc. of the subject's blood, one simply divides 33.25 by the weight of carbon dioxide

TABLE 1.—*Comparison of the Concentration of Alcohol in the Blood and in the Breath as Determined from the Ratio of Alcohol to Carbon Dioxide and from Simple Volume*

Subject Number	Alcohol in the Blood, Mg. per Cc.	Alcohol in the Breath: Pump, Mg. per 100 Mg. of CO_2	Balloon, Mg. per 100 Mg. of CO_2	Balloon, Mg. per 4 Liters of Expired Air
1	1.46	1.58	1.36	No analysis
2	2.00	1.75	1.95	No analysis
3	2.45	1.52	1.69	No analysis
4	0.78	0.81	0.65	0.83
5	2.25	2.05	1.79	2.69
6	1.94	2.08	1.82	1.89
7	3.25	3.19	2.16	3.33
8	3.00	2.72	2.91	3.18
9	1.18	0.97	0.95	1.27
10	1.07	1.00	1.20	1.67
11	1.59	1.47	1.61	2.06
12	1.99	1.63	2.02	1.89
13	1.13	1.52	1.04	1.40
14	2.82	1.98	2.02	2.06
15	2.54	2.30	2.34	2.18
16	1.78	No analysis	2.02	1.75
17	3.00	2.51	No analysis	1.75
18	3.48	2.41	No analysis	3.34
19	1.19	No analysis	1.40	1.75
20	1.29	No analysis	1.87	1.75
21	2.93	2.41	2.24	2.33
22	1.58	No analysis	1.72	1.40
23	2.80	2.84	1.71	2.18

contained in the sample of breath which served just to decolorize the purple fluid.

This figure may be checked by calculating the weight of alcohol in 4 liters of the sample of breath, since we have confirmed the observation of Bogen[9] that the breath as collected usually contains about 50 per cent of alveolar air. It will require 700 cc. of a breath containing 1 mg. of alcohol in 4 liters to remove the color from 1 cc. of the permanganate solution. Then, 700 ÷ cc. of breath used = mg. of alcohol in 4 liters of expired air or in 1 cc. of blood.

RESULTS OF THE BREATH METHOD AS COMPARED WITH BLOOD ANALYSIS

In order to determine how closely the concentration of alcohol in the blood can be predicted from the ratio of alcohol to carbon dioxide in the breath, as computed by our method, tests were conducted on 121 persons admitted to the Indianapolis City Hospital. Most of these subjects had been involved in accidents and represented various degrees of alcoholism. The sample of breath was taken from about one half of the subjects by means of the pump and from the remainder by means of rubber balloons. We obtained specimens of blood also from all these subjects, drawn within five minutes of the time the breath was analyzed. The blood was analyzed for alcohol by a micromethod recently published by one of us.[19] The intern who operated the breath apparatus and drew the specimen of blood also recorded the subject's symptoms relative to intoxication; the symptoms were recorded before the final report of the analyses of the breath and the blood was received. The results obtained in this study are shown graphically in figure 5. The data show some scattering but the average correlation is good, and in practically all of the cases the figures obtained for the breath and for the blood gave essentially the same information regarding intoxication. With part of the subjects we used both balloon and pump, and in some cases in which the balloon was used we measured the specimen of breath passed through the apparatus by collecting it over water in a gas buret. These results are given in table 1. The data indicate that the pump and the balloon gave almost identical results and that satisfactory figures were obtained by simply measuring the volume of breath used.

INTERPRETATION OF RESULTS OF CHEMICAL ANALYSES

It is a well established fact that the degree of intoxication may be predicted fairly closely from the level of alcohol in the body. In a recent review of this subject, Emil Bogen[20] stated: "The accumulated records of literally thousands of instances where the signs and symptoms of alcoholic intoxication have been correlated with the concentration of alcohol in the blood and tissues have conclusively shown that they go hand in hand." In addition to twenty-three references cited by Bogen, we might mention the work of Remund,[21] Jungmichel,[22] Schwarz[23] and Hoffmann,[24] all of whom reached the same conclusion. In table 2 we have collected the statistics from extensive studies by Widmark,[25] Schwarz[23] and Bogen,[9] as well as some unpublished results from our laboratory, which compare the chemical results with independent clinical observations. Both Widmark and Schwarz have emphasized that the criterion of "under the influence" probably varied considerably among the large number of examining physicians, and also that the use of exact laboratory procedures would frequently have revealed impairment of driving ability in borderline cases in which persons were adjudged sober. In a private com-

TABLE 2.—*Correlation of Intoxication with the Concentration of Alcohol in the Body at Various Levels (Percentage of Subjects Clinically "Under the Influence of Alcohol")*

Alcohol Concentration (Parts per Thousand)*	Widmark, Blood (562)†	Schwarz, Blood (905)	Harger, Blood and Breath (140)	Bogen, Urine (250)	Bogen, Breath (100)
0-0.5	None	2	None	None‡	15‡
0.5-1.0	23	38	46	50‡	50‡
1.0-1.5	49	93	50		
1.5-2.0	80	97	92	66‡	85‡
2.0-2.5	95	99	100		
2.5-3.0	100	100	100	88‡	92‡
3.0-3.5	100	100	100		
3.5-4.0	100	100	100	97‡	100
4.0-4.5	100	100	100		
4.5-5.0	100	100	100	100	100
Above 5.0	100	100	100		

* One part per thousand equals 1 mg. per gram, or 0.1 per cent.
† Number of subjects given in parentheses.
‡ Definitely drunk. Figures for "under the influence of alcohol" should be considerably higher. (See explanation in text.)

19. Harger, R. N.: A Simple Micromethod for the Determination of Alcohol in Biologic Material, J. Lab. & Clin. Med. **20**: 746 (April) 1935.

20. Bogen, Emil: Tolerance to Alcohol: Its Mechanism and Significance, California & West. Med. **44**: 262 (April) 1936.
21. Remund, M. H.: Gerichtlich-Medizinische Erfahrungen und Probleme bei Automobilunfällen, Habilitationsschrift, Basel, Schwabe u. Co., 1931.
22. Jungmichel, Gottfried: Alkoholbestimmung im Blut: Methodik und forensische Bedeutung, Berlin, C. Heymann, 1933.
23. Schwarz, Fritz: Einige Erfahrungen bei der Durchführung der quantitativen Alkoholbestimmung, Schweiz. med. Wchnschr. **67**: 54 (Jan. 16) 1937.
24. Hoffmann, Kurt: Alkoholnachweis bei Verkehrsunfällen, Berlin, Urban & Schwarzenberg, 1937.
25. Widmark, E. M. P.: Die theoretischen Grundlagen und die praktische Verwendbarkeit der gerichtlich-medizinischen Alkoholbestimmung, Berlin, Urban & Schwarzenberg, 1932.

munication Dr. Bogen stated that the percentages quoted in his paper represent persons who were definitely drunk and that the percentages of persons "under the influence of liquor" were considerably higher.

An examination of table 2 will show that, while there is a good correlation between the level of alcohol in the body and intoxication, this correlation is not perfect. As pointed out by Widmark [25] and others, there is a zone, in which the concentration extends from about 0.8 part of alcohol per thousand up to 1.5 parts of alcohol per thousand (from 0.08 to 0.15 per cent by weight), in which a diagnosis of "under the influence of alcohol" would not apply in all cases. In this zone the probability of a person's being under the influence of alcohol increases with rise in the level of alcohol in the body. A careful study of the literature, as well as our own observations, has convinced us that all subjects having a level of alcohol in the body above 1.5 parts per thousand (0.15 per cent) are sufficiently impaired to be unsafe automobile drivers and that a level above 1.5 parts per thousand should be prima facie evidence that the person is under the influence of alcohol. When one applies Widmark's factor r,[25] which means the ratio of the alcohol in the blood to the alcohol in the entire body, a level in the blood of 1.5 parts per thousand corresponds to an accumulation of from 3 to 3½ ounces (90 to 105 cc.) of alcohol, or from 6 to 7 ounces (180 to 210 cc.) of whisky, in the body of a person weighing 150 pounds (68 Kg.). When the level of alcohol in the blood is between 0.8 and 1.5 parts per thousand this fact should be recorded and used as additional evidence if the usual symptoms of alcoholism are present.

The maximum concentration of alcohol which should be permitted in the body of an automobile driver depends on the definition of "under the influence of alcohol." Miles,[26] Heise,[27] Schmidt,[28] Elbel [29] and others [30] have shown that concentrations even lower than 0.8 part per thousand, which are usually insufficient to produce gross symptoms of intoxication, are capable of reducing the driving efficiency of many people. This point was stressed in a recent report by the American Medical Association's committee for the study of motor vehicle accidents.[31]

COMMENT

With subjects having high concentrations of alcohol in the body our results indicate a tendency for the weight of alcohol in the breath accompanying 190 mg. of carbon dioxide to be somewhat lower than the amount of alcohol per cubic centimeter of blood. This may be due either to a depression of the respiratory center, resulting in elevation of the carbon dioxide tension in the blood and the alveolar air, or to the test's passing the end point of the purple fluid on account of the small volume of breath used. The second explanation is indicated by data secured by omitting the permanganate solution and analyzing the alcohol absorbed by the sulfuric acid by our microdichromate method.[19] Most of our determinations were done with 0.5 cc. of the permanganate solution, and we believe that increasing the amount to 1 cc., according to the directions given, will help to eliminate errors due to passing the end point. While the measurement of the volume of breath required to decolorize the purple fluid gave satisfactory results, we feel that this should be checked by determination of its carbon dioxide content. The latter procedure is of course necessary with subjects who will not or cannot cooperate.

As pointed out by Bogen,[9] nonalcoholic subjects who simply rinse out the mouth with a strong alcoholic beverage such as whisky will exhibit alcohol in the breath for a short time afterward. However, as shown by Bogen and confirmed by ourselves, this effect is almost gone in five minutes and entirely disappears after about ten minutes. For this reason a period of at least ten minutes should elapse between the taking of alcoholic fluids into the mouth and the collection of the breath. In the practical testing of automobile drivers this source of error seems unimportant, but it should certainly be recognized by persons using the method.

Although the preliminary test and most of the quantitative procedure may be carried out by a person with little chemical training, we strongly urge that persons using the method have the assistance of a local chemist, who can weigh the Ascarite tubes and check the composition of the solutions. Whenever possible the subject should be examined by a physician, and the employment of a competent physician or toxicologist will greatly aid in presenting the case in court.

The method described in this paper will probably not predict the concentration of alcohol in the brain quite as closely as analysis of blood, but we believe that the results are amply accurate for practical purposes. In addition to being used in medicolegal cases, it may aid, when the pump is used, in differentiating alcoholic coma from coma due to other causes.

The Indiana State Police and Dr. Preston M. Nesbit of Arlington, Texas, cooperated in trying out the method with automobile drivers. In the experiment conducted by the Indiana State Police, most of the persons who the test indicated were under the influence of alcohol pleaded guilty, and in most cases in which the defendant did not plead guilty the evidence of the test was accepted by the courts and convictions resulted. In a recent communication Dr. Nesbit reported the use of the test on ninety-three automobile drivers suspected of being under the influence of alcohol. Of these, seventy-nine were declared to be under the influence of alcohol on the basis of the test and physical appearances, and all pleaded guilty.[32]

It should be emphasized that chemical tests for intoxication should not exclude evidence such as observations of eyewitnesses and physical tests but that chemical tests will give additional information, which is often sorely needed. Such tests will exonerate the nondrinker and even the mild drinker, and they will show the concentration of alcohol in the drinker's brain.

SUMMARY

1. A reagent for alcohol in the breath consists of 55 per cent sulfuric acid containing a small measured amount of permanganate solution. The permanganate reacts rapidly and quantitatively with alcohol at ordinary temperatures and is not affected by acetone.

26. Miles, W. R.: Alcohol and Human Efficiency: Experiments with Moderate Quantities and Dilute Solutions of Ethyl Alcohol on Human Subjects, Publication 333, Washington, D. C., Carnegie Institution of Washington, 1924.

27. Heise, H. A.: Alcohol and Automobile Accidents, J. A. M. A. **102:** 739 (Sept. 8) 1934.

28. Schmidt, Max: Concentration of Alcohol in Blood, J. Indust. Hyg. & Toxicol. **16:** 355 (Nov.) 1934.

29. Elbel, Herbert: Blutalkoholkonzentration und Alkoholwirkung, Deutsche Ztschr. f. d. ges. gerichtl. Med. **28:** 64 (March) 1937; Zur Frage der Bewertung von Blutalkoholbefunden, München. med. Wchnschr. **84:** 1133 (July 16) 1937.

30. Effects of Alcohol on Drivers of Motor Vehicles, Berlin Letter, J. A. M. A. **109:** 1376 (Oct. 23) 1937.

31. Preliminary Report of Committee to Study Problems of Motor Vehicle Accidents, J. A. M. A. **108:** 2137 (June 19) 1937.

32. Two of these drivers at first pleaded not guilty and appealed their cases to the District Criminal Court, but they changed their pleas to guilty before their cases were tried.

2. The ratio of alcohol to carbon dioxide in the breath may be used to measure the concentration of alcohol in the blood. The weight of the alcohol accompanying 190 mg. of carbon dioxide in the breath is very nearly equal to the weight of the alcohol in 1 cc. of the subject's blood.

3. Employment of the ratio of alcohol to carbon dioxide in the breath permits the test to be done without the subject's being touched. A tube is held in the breath stream and a pump draws the sample through the apparatus.

4. Tests made on 121 subjects showed a good correlation between the concentration of alcohol in the blood and the amount of alcohol accompanying 190 mg. of carbon dioxide in the breath.

5. As collected in our tests, 4 liters of expired air contained about the same amount of alcohol as 1 cc. of the subject's blood. Because of possible fluctuations in the amount of alveolar air in such samples, it is believed that analyses of breath made on the volume basis should be checked by determining the carbon dioxide in the sample.

FACTORS IN THE MORTALITY RATE OF ARTERIOSCLEROTIC GANGRENE

A COMPARATIVE STUDY OF 214 CASES OF SURGICAL INTERVENTION

JAMES ROSS VEAL, M.D.

NEW ORLEANS

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The various persons and groups of persons who have devoted themselves within the last few years to the subject of peripheral vascular disease in its many manifestations have merited the highest praise. The results which they have achieved have in themselves been brilliant and have had the further effect of bringing to the forefront of medical consciousness, as it were, a group of diseases formerly relegated to the background because their prognosis was so hopeless.

Particularly in the obliterative type of peripheral vascular disease, however, all these recent endeavors have been on the prophylactic side and have had as their basic purpose a prompter anticipation and recognition of the impending terminal gangrene, with the institution of active measures to avoid its development. This is as it should be, for prophylaxis is always more to be desired than curative therapy. Yet there is another side of the picture, which must not be forgotten. One gains nothing by not facing the fact that even a more general adoption of prophylactic measures will not produce the millenium as far as peripheral vascular diseases of the obliterative type are concerned. The occasional private patient and probably the majority of public charges will continue to exhibit some degree of terminal gangrene, and a large number of the latter will probably continue to exhibit massive gangrene. There is no doubt therefore that physicians should continue to devote their attention to this sorry subject and should continue their attempts to improve results in the management of the terminal state.

Two years ago McFetridge and I [1] published from the New Orleans Charity Hospital for the five year period ended in 1933 an analysis of 171 amputations for primary vascular disease of the extremities, for which the mortality was 39.1 per cent (sixty-seven cases). In the group were 110 cases of arteriosclerotic gangrene, in which the mortality was 39 per cent (forty-three cases). During the last three and a half years 104 amputations for the same condition were performed in the same institution by essentially the same group of surgeons and, presumably, on essentially the same type of subject. The mortality in the second series was 28.8 per cent (thirty cases), which, although still intolerably high, is materially lower than in the first series, and the reduction seems worthy of investigation.

It might be well, before entering on this analysis, to make certain general statements about arteriosclerosis. It is a systemic disease which implies a generalized degeneration of the whole vascular tree. Gangrene is merely a localized manifestation of systemic pathologic change, a local warning, if I may so express it, of generalized vascular deficiency. The underlying vascular change is an obliterating endarteritis that affects all the vessels of the body from the thoracic aorta to the finest radicles. The nongangrenous parts of the vascular tree are still in a state of compensation, but the margin of safety is slight, and undue strain or stress—such as might be supplied by amputation of the local affected area, for instance—may bring about failure of the entire system. The vital organs, particularly the kidneys, the myocardium and the brain, have been so injured by impairment of the circulation that they are literally in a state to which the term "locus minoris resistentiae" may properly be applied.

If these facts are accepted, as they must be by all thinking surgeons, it is clear that the systemic reaction in arteriosclerotic gangrene is considerably more important than the local reaction. It is clear also that arteriosclerotic gangrene carries per se a certain inevitable death rate. But it is equally clear that failure to comprehend the systemic nature of the disease will add to that death rate, while due regard for it is likely to lower the mortality. Furthermore, certain definite factors, some controllable by the physician and some by the patient, also have their part. These include the extent and the duration of the gangrene, its exciting cause, the age of the patient, the presence of a systemic febrile reaction before operation, the site of amputation and the development of recurrent gangrene, infection or slough of the stump. All these factors are important in varying degrees, but it is not too much to say that not one of them is as important as is the preoperative and postoperative management of the patient. Indeed, one may go further and make the unqualified statement that by the attention he devotes to this particular phase of therapy the surgeon expresses his regard for and comprehension of the patient's systemic disease.

The extent of the gangrene has a twofold significance: It bears a direct relation to the degree of vascular occlusion, and it also is an index of the duration of the process. Since arteriosclerotic gangrene is known to spread slowly, it may reasonably be assumed that a patient who has gangrene confined to one toe or several toes either has less vascular occlusion or a disease of shorter duration than a patient who has gangrene involving the entire foot. In only ninety-one of the total of 214 cases in both series was the gangrene still confined to the toes, and it is not surprising to find that in this group the mortality was only 29.6 per cent (twenty-seven cases), as compared to a mortality of

From the Louisiana State University School of Medicine and Charity Hospital.

1. Veal, J. R., and McFetridge, E. M.: The Surgery of Gangrene of the Extremities: With a Study of 171 Cases from the Records of Charity Hospital in New Orleans, Surg., Gynec. & Obst. **60**: 840-847 (April) 1935.

48.5 per cent (thirty-four cases) for the group of seventy cases in which the gangrene involved half or more of the foot.

It is clear from these figures that delay is one of the most important controllable factors in the treatment of arteriosclerotic gangrene. On the part of the patient it may be at least partially controlled by educational methods. A person who is under a physician's care

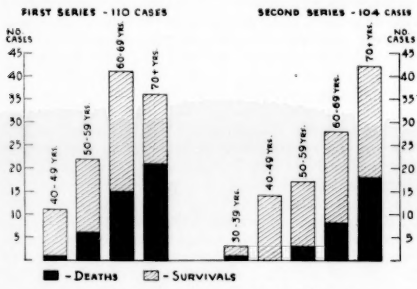

Chart 1.—Age as a factor in the mortality rate.

for arteriosclerosis should be warned whenever the opportunity arises of the hazards of gangrene and should be made to realize that when once it has set in prompt treatment is life saving. It is obviously impossible to warn patients who do not submit themselves to medical treatment for their systemic disease, and it is just as well to face the fact that patients of the general level of intelligence seen in Charity Hospital and in similar public institutions will be likely always to present themselves late.

But the delay is not always the patient's fault. He may present himself late for treatment, he may refuse operation when it is offered, but it is not always offered. At least part of the mortality due to delay must be charged against the physician who, because of carelessness or from the worthier, though no less dangerous, motive of conservatism, postpones employment of radical measures beyond the limits of safety. Often, of course, the physician finds himself on the horns of a dilemma. All his instincts are against mutilating surgery; all his instincts are to practice conservatism. But when public charges, of a generally low level of intelligence and with the advanced type of disease that inevitably follows, are in question, conservatism is frequently neither practical nor safe. Usually the attempt at salvage fails, and frequently the patient pays for it with his life. To quote from our earlier paper on this subject: "The surgeon who procrastinates, no matter how worthy his motives may be, adds to the death rate in gangrene just as surely as does the patient who delays presenting himself for treatment or who refuses surgery when it is offered to him."

Arteriosclerosis is a progressive disease. It develops in middle life or later as a rule, and as the patient grows older progressively greater destruction of the vascular bed occurs, with, as I have pointed out, progressively greater involvement of the vital organs, particularly the heart, the kidneys and the brain, as well as the peripheral blood vessels. It is clear then that the older the patient is when his gangrene develops the poorer the surgical risk he presents. On the other hand, an analysis from the standpoint of age of the two series of amputations at Charity Hospital offers no explanation of the more than 10 per cent difference in the mortality rates. The average age of the 110 patients in the first series was 64.2 years and of the 104 patients in the second series 63.6 years. A variation of less than a year in age cannot logically be invoked to explain a variation of more than 10 per cent in mortality.

Chart 1 is a graphic presentation of the mortality rates by decades in the two series. If one disregards the patients under 40 years of age, who do not appear at all in the first series and are too few in the second to warrant any deductions, two tendencies are plain, the increase in the death rate in both series with advancing age and the materially decreased death rate in the younger groups in the second series. There is practically no difference, as I have said, in the age of the patients in the two series, but it is not surprising to find the average age of death in the first series 67.8 years, more than three years higher than the average age for the whole group (64.2 years), and in the second series 69.3 years, almost five years higher than the average age for the whole group (63.6 years).

It is entirely reasonable that the exciting cause of the gangrene should definitely influence the mortality rate and that spontaneous gangrene should carry a higher death rate than the traumatic variety. Many patients in whom trauma is the exciting cause have an adequate peripheral circulation in spite of their disease. The trauma is accidental and extrinsic. Their general condition therefore is better, their vital organs are less seriously damaged and they have a correspondingly greater chance of survival than the patients in the other group, whose gangrene has developed spontaneously as a result of their disease. It is not necessary to labor the point that in this second group the arteriosclerosis is more severe and the arterial obliteration more extensive. Practically all such patients give a history extending over months or even years of such preliminary signs and symptoms as cold feet, ischemic pain at night, changes in color and intermittent claudication. In the first series the mortality for traumatic gangrene was 32.5 per cent, against 40.4 per cent for spontaneous gangrene, and in the second series the mortality for traumatic gangrene was 16.6 per cent, against 37.7 per cent for the spontaneous variety. Again, in addition to the marked difference that was observed between the two varieties of gangrene, the drop in the general death rate occurring in the second series should be noted.

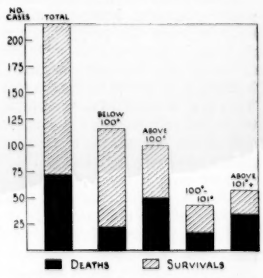

Chart 2.—Relation of preoperative fever to mortality rate.

To avoid misunderstanding, it might be well to call attention to one exception to the statements I have just made. In the so-called arteriolosclerotic disease spontaneous gangrene of the toes may occur early, while other parts of the cardiovascular system may in general be entirely adequate. This, however, is a specific type of arteriosclerosis, and its particular phenomena do not invalidate the points I have made concerning the etiologic factor in arteriosclerotic disease.

The susceptibility to infection of the patient with diabetic gangrene is generally realized. It is not so generally realized, however, that the arteriosclerotic subject manifests the same susceptibility, although in a more sluggish manner. As we pointed out in our previous communication on this subject, infection in the arteriosclerotic patient is deep seated, a sort of underground process that spreads along tissue planes and only rarely manifests itself in a true line of demarcation. If it is not actually present it is potentially present. The gangrene may begin as a dry type, in contradistinction to the moist type of diabetic gangrene, but infection is only a matter of time, and, just as in the diabetic patient, the infection increases the gangrene and the gangrene increases the infection.

It is true that the constitutional reaction is not so marked in the arteriosclerotic as in the diabetic patient. The former shows his toxicity chiefly as a lack of well being. He manifests indifference to the intake of food and fluid, reduction of the liquid output, listlessness and drowsiness that at times approach actual stupor, and often a mild senile dementia that is indicative of involvement of the cerebral vessels. I have been particularly impressed by this picture in the Negro men's wards, and, as I shall point out shortly, the improvement in results has been most gratifying since my co-workers and I have realized its significance and endeavored to correct it.

Infection associated with a febrile reaction apparently has an important bearing on the mortality rate when it is present prior to amputation (chart 2). In the first series, fifty-five of 110 patients had a temperature of 100 F. or more before operation, and thirty-two, or 58.1 per cent, died. In the second group, forty-four of 104 patients had a temperature of 100 F. or above before operation and eighteen, or 40.8 per cent, died. In the first series thirty-nine patients had a temperature of 101 F. or more before operation, of whom twenty-six, or 66.6 per cent, died. In the second group eighteen had a temperature of 101 F. or more before operation, of whom seven, or 38.8 per cent, died. The lowered mortality in the second series was unquestionably due to a fuller comprehension of the dangerous state of the patients, and, as I shall point out shortly, correspondingly more careful preparation.

Combining the figures for the two series, one finds that ninety-nine of the total of 214 patients had a febrile reaction with a temperature of 100 F. or more before operation and that fifty, or 50.5 per cent, died. Fifty-seven had a temperature of 101 F. or more, of whom thirty-three, or 57.8 per cent, died. The influence of infection on the death rate can be illustrated even more clearly by the reverse of this picture. Of the 115 patients in whom no febrile reaction existed before operation, only twenty-three, or 20 per cent, died. It seems scarcely necessary to add that the longer the toxemia existed the higher was the mortality; arteriosclerotic subjects, and particularly aged subjects, do not tolerate infection well.

The question of where to amputate in cases of primary vascular gangrene is perhaps the most controversial question regarding the management in such cases. Here again the surgeon is on the horns of a dilemma. He does not wish to amputate higher than is actually necessary, not only for economic and cosmetic reasons but because, other things being equal, the higher the amputation the higher the mortality. Yet if he amputates too low and the circulation in the area proves inadequate, the patient runs the chance of recurrent gangrene, which carries with it a risk many times higher than the original risk.

The proportion of amputations at the various sites (chart 3) is widely different in the two series under discussion, as is the distribution of the mortality, and it is worth while to consider these differences in detail. In the first series the mortality for amputations of the toe was 11.7 per cent (seventeen cases with two deaths), against 16.6 per cent in the second series (six cases with one death), the smaller number of cases in the second series obviously making the comparison unsound. In the first series the mortality for amputations of the leg was 34 per cent (forty-seven cases with sixteen deaths), against 20.6 per cent in the second series (twenty-nine cases with six deaths). In the first series the mortality for amputation at the thigh was 55.5 per cent (forty-five cases with twenty-five deaths), as compared with a mortality of 33.3 per cent in the second series (sixty-nine cases with twenty-three deaths). What is responsible for the marked decrease in the mortality of the second series, in which actually the proportion of presumably lethal amputations at the thigh was far higher than in the first series?

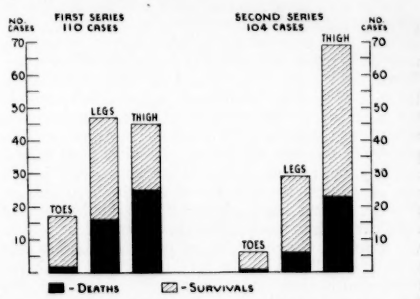

Chart 3.—Mortality in relation to site of amputation.

Undoubtedly the reason for the lowered mortality for the more dangerous operation was a more careful selection of cases, a more uniform endeavor to determine the lowest level of adequate circulation. That endeavor, regrettably, was still not entirely uniform, but there was a marked improvement over the frankly haphazard methods of the first series. There is still, of course, no general agreement as to how the level of adequate circulation is to be determined. Age is not a safe guide, nor is the gross appearance of the limb. My co-workers at the Charity Hospital and I agree with McKittrick [2] that the only adequate clinical sign is the presence of palpable popliteal and tibial pulses. If these are missing other methods must be resorted to, most of which are still too intricate to be used by surgeons who do not have access to the facilities of a well equipped hospital. Arteriography,[3] which we feel is the most adequate method, falls into this category. It cannot be used as a matter of routine and it is of value only in the hands of men who use it regularly and who have had a wide experience with it. The

2. McKittrick, L. S.: Indications for Amputation in Progressive Arterial Obliteration of the Lower Extremities, Ann. Surg. **102**: 342-350 (Sept.) 1935.

3. Veal, J. R., and McFetridge, E. M.: Adequate Circulation in Extremities: Arteriography as a Test for Determining Limits, J. A. M. A. **104**: 542-545 (Feb. 16) 1935.

histamine test, as compared with it, has not been satisfactory in our hands, but the salt absorption test of McClure and Aldrich,[4] which we have used frequently during the last three years, seems reliable.

The test is so simple that it is susceptible of general use. Intradermal injections of 0.2 cc. of physiologic solution of sodium chloride are made at 3 inch intervals on the inner aspect of the leg from the ankle to the upper third of the thigh, the rate of absorption of the resulting wheals being used as an index of the adequacy of the circulation at each level. When the circulation is normal the rate of absorption is slow and the wheals persist for an hour or more. When the circulation is impaired the rate of absorption is uniformly increased from above downward; some of the wheals are completely absorbed at the end of five minutes. As we have employed the test, we regard the circulation as adequate at and above a given level if the wheal at that level is half of its original size at the end of an hour.

It must be remembered that the mere existence of adequate circulation at a certain level by no means guarantees primary healing. Primary healing, for instance, occurred in only thirty-five of the fifty-four patients in both series who survived leg amputations.

Other considerations, too, enter into the question of primary healing, notably certain points in operative technic. We consider the circular type of amputation most satisfactory and used it in practically all our cases. Speed, while both desirable and essential, especially in the case of aged and debilitated patients, does not take the place of careful technic. Ragged incisions and trauma to the tissues will further impair the already precarious terminal circulation. Bleeders must be tied securely, but hemostasis should not be achieved by the use of sutures through the muscle layers. Sutures through the muscles, fascia and skin should be tied just tightly enough to approximate the layers; undue tension will result in slough or further gangrene. Every surgeon is familiar with the type of case in which the circulation is apparently adequate at the level selected for amputation but in which, because tight mass sutures were applied, the terminal vessels were completely cut off and gangrene of the stump resulted.

The status of the circulation at the site of amputation is, as I have said, the most important basic factor in determining primary healing. If it is inadequate, recurrent gangrene or massive sloughs will almost inevitably result. In the first series the incidence of recurrent gangrene in cases of amputation of the toes was 47 per cent (eight of seventeen cases), against 50 per cent in the second series (three of six cases), which is not materially different. In the first series the incidence in cases of leg amputation was 34 per cent (sixteen of forty-seven cases), against 27.5 per cent in the second series (eight of twenty-nine cases). In the first series the incidence in amputations at the thigh was 8.9 per cent (four of forty-five cases), against 5.7 per cent in the second series (four of sixty-nine cases). In addition to the decreased incidence in the second series in both leg and thigh amputations, the high proportion of recurrence of the gangrene in both series when amputation of the toes was done is striking in contrast to the low incidence in both series when amputation at the thigh was employed. Such contrasts prove again the dangers of conservatism in the treatment of this disease and suggest that at least in some cases the risk of a higher mortality for a more dangerous operation may be justified; it must not be forgotten that reamputation for recurrent gangrene carries an almost prohibitive mortality.

Gas gangrene as a complication of amputation has been particularly emphasized by Eliason and Callendar, but with us [5] it has not been an outstanding problem. This is rather surprising because of our high proportion of Negro patients (149 of the total 214) and their known predilection for this special type of infection. Certainly our overcrowded wards and the Negro's elementary ideas of personal hygiene would seem to make him a fit subject. The incidence may perhaps be higher than we realize, for we have not practiced making routine cultures of material from infected stumps or stumps which exhibit recurrent gangrene. On the other hand, this type of infection is so distinctive that we doubt that we have overlooked many cases.

As is usual after amputation, most stumps in both series showed some exudation of serum, and a regrettably large number showed some degree of infection. It must not be assumed that such phenomena are part of the normal healing process. They are not. Both exudation and infection, however mild they may be, produce some swelling of the tissues, which in turn reduces the supply of blood to the part and may eventually lead to serious trouble. The temperature and the pulse rate are not reliable indexes of the presence or absence of infection in the stump. Direct observation is necessary and daily dressings must be a matter of routine. If swelling produces the slightest tension on the sutures they must be promptly removed, and active measures must be taken at the first sign of infection. Infection of the stump is not infrequently associated with thrombophlebitis and lymphangitis, and these local conditions may serve as a focus of infection elsewhere, which is a point not usually considered.

There is no question in our own minds but that the most important single factor in the decreased mortality in the second series of amputations for arteriosclerotic gangrene was the careful and systematic preoperative and postoperative management which most of these patients received as compared with the hit and miss preparation and after-care which many of the patients in the first series received. The change in management was based on the new conception of arteriosclerotic gangrene, which I have already emphasized, that it is a systemic consideration first and a local consideration second. As a rule the patient at Charity Hospital with this type of gangrene is admitted from several weeks to several months after it has developed. He is likely to be poorly nourished, dehydrated and toxic, and he has other liabilities; usually he is an old man—even the patients in middle life tend to be much older organically than their actual years—and he has the disabilities of age, chiefly cardiac and renal disease, associated with a general weakening of his vital powers. Even with adequate preparation such patients are often not good surgical risks, and without adequate preparation amputation is many times equivalent to execution. Failure to realize the significance of these facts was at least partially responsible for the high mortality in the first series, while its rather general realization was undoubtedly responsible for the lowered death rate in the second.

The method of preparation and after-care needs no detailed description. There is no undue delay in opera-

4. McClure, W. B., and Aldrich, C. A.: Time Required for Disappearance of Intradermally Injected Salt Solution, J. A. M. A. **81**: 293-295 (July 28) 1923.

5. Veal, J. R.: Study of Gas Bacillus Infection, with Special Reference to Its Occurrence in the Negro, New Orleans M. & S. J. **89**: 432-437 (Feb.) 1937.

tion, and preparation for it is begun immediately in those cases in which it is indicated. A perverted water balance is corrected by the free use of fluids. Renal function is estimated and the urinary output is improved. The cardiac reserve is tested and medical consultation sought as necessary. Infusions of dextrose solution are a routine preoperative measure. As a result of these precautions the majority of patients stand operation well. Similar treatment is continued postoperatively as long as it is necessary. Special attention is paid to the use of infusions of dextrose solution and other methods to prevent and combat shock, and transfusion is employed as the need arises. The patients are moved about in bed after operation and gotten up in chairs at the earliest possible moment, to forestall respiratory complications. As a result of these measures the patients in the second series were, case for case, far better surgical risks than the patients in the first series, though their gangrene, generally speaking, was no less extensive and their systemic disease was no less severe.

I have already discussed the importance of watching for and treating even mild infections after operation, and it remains to mention one other precaution. Every effort should be made to maintain the circulation of the stump at its optimum level, which is not achieved, in my opinion, by the usual practice of elevating it on a pillow at a level higher than the heart. I believe that a reverse plan should be followed and passive venous congestion produced by placing the stump lower than the level of the heart. This is best accomplished by placing it on a thin, soft pillow and elevating the head of the bed 12 inches. A heat cradle is also used, the temperature of which at the level of the stump should not be higher than 100 F.

With the change in the general management and the consequent reduction in the mortality, it is of interest to compare the causes of death in the two series. In chart 4, *A* and *B* are graphic presentations of the proportionate distribution of the causes of death in the two series, and chart 4 *C* is a composite picture of the causes of death in thirty cases in which autopsy was done. It will be noted that the latter corresponds closely to the clinical analyses of the causes of death.

Three marked differences are immediately apparent: a marked reduction in the proportion of deaths from complications involving the kidneys, a marked reduction in the proportion of deaths from shock and a rather marked rise in the proportion of deaths from cardiac failure.

The reduction in the number of deaths from kidney disease (most often acute or chronic nephritis, with or without uremia) and from shock has unquestionably been brought about by the improved preoperative and postoperative care, on which I have already commented. Particularly important in this connection is the free use of fluids in the form of hypodermoclysis and infusion. Yet the rise in the proportion of deaths from cardiac failure is disquieting and warrants investigation. In this category are included the cases of congestive failure and coronary thrombosis in which the cardiac reserve is low; and the added stress and strain of surgical intervention, no matter how careful the preparation, may be enough to turn the tide against the patient. Also included are the cases in which the cardiac reserve may be sufficient to withstand the strain of operation but not the added toxemia from infection of the stump. Another disappointing type of case included, which is unfortunately familiar to all surgeons, is that in which the patient passes safely through the ordeal of operation, only to succumb to cardiac failure when he resumes his activity.

I am particularly concerned in this group of deaths with the patients who died of cardiac failure associated with acute pulmonary edema. Not inconceivably some of those deaths were due to the very measures adopted to reduce the proportion of deaths from kidney diseases and from shock. The pulmonary edema might reasonably have been produced by a too liberal use of salt solution. The work of Coller, Dick and Maddock [6] on this type of edema is enlightening, and their suggestion that dextrose be substituted for an excess of saline solution could well be followed in treating aged arteriosclerotic subjects.

The small reduction in the number of deaths from pneumonia is encouraging and is probably due to a reduction in the incidence of the hypostatic type of disease. It is not surprising, in view of the age of the patients, that pneumonia should continue to be the principal cause of death. At their period of life chronic bronchial infections are frequent, and few patients of the social stratum included in this report are free from dental sepsis.

There is reason to believe too that in some cases pneumonia may be due to showers of emboli from the amputated stump. In many cases the onset and the clinical course suggested an embolic rather than an infectious origin, and in some cases, when x-ray examinations were made early in the course of the illness, multiple small shadows suggesting infarcts were revealed.

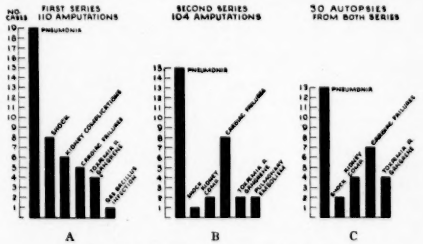

Chart 4.—Causes of death after operation.

SUMMARY

1. Arteriosclerotic gangrene is the local manifestation of a systemic disease.

2. Factors in the mortality include the extent and duration of the gangrene, its exciting cause, the age of the patient, the presence of a systemic febrile reaction before operation, the site of amputation, the development of recurrent gangrene, infection or sloughs after operation and, most important of all, the preoperative and postoperative measures employed. The last consideration, although it is not generally realized, is quite as important in treating the arteriosclerotic patient as in treating the diabetic patient.

3. In two series of amputations for arteriosclerotic gangrene, including, respectively, 110 and 104 cases, analyzed in detail from the standpoint of these factors, the mortality in the second was more than 10 points lower than that in the first.

6. Coller, F. A.; Dick, V. S., and Maddock, W. G.: Maintenance of Normal Water Exchange with Intravenous Fluids, J. A. M. A. **107**: 1522-1527 (Nov. 7) 1936.

VAGINAL TAMPONAGE FOR CATAMENIAL SANITARY PROTECTION

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Temporary vaginal tamponage for the purpose of collecting the catamenial discharge has been practiced by women of certain professional groups, such as acrobats and dancers, who cannot wear the usual sanitary pad because of visibility through their costumes. Many of these women, however, have abandoned tampons for small vulval pads which are inserted between the lips of the vulva and collect the exudate during the short interval in which they require such protection. Self tamponage has within the last few years been advocated by a few tampon manufacturers, and tampons have been used for catamenial sanitary protection in place of the usual sanitary pads. The purpose of our investigation was to determine the efficiency of tampons in collecting the catamenial discharge of normal women.

TABLE 1.—*Data on an Average Normal Woman*

Subject: Stenographer, aged 30, height 5 feet 6 inches (167.6 cm.), weight 135 pounds (61 Kg.). Weight of each pad 11.9 Gm., weight of each tampon 3.7 Gm.

Number of Tampon and Pad	Hours Worn	Total Amount Absorbed, Gm.	
		Tampon	Pad
1	5:30 a.m. to 11:00 a.m.	2.7	0.2
2	11:00 a.m. to 4:00 p.m.	11.8	4.1
3	4:00 p.m. to 11:00 p.m.	11.3	1.1
4	11:00 p.m. to 7:00 a.m.	11.3	1.1
5	7:00 a.m. to 10:00 a.m.	8.0	0.4
6	10:00 a.m. to 4:00 p.m.	5.4	0
7	4:00 p.m. to 10:00 p.m.	10.0	1.1
8	10:00 p.m. to 7:00 a.m.	0.8	0
9	7:00 a.m. to 4:00 p.m.	5.3 (mostly urine)	0
Total		66.6	8.0

Ninety-five women were studied, and three different makes of tampons were purchased and used in the experiments.

Tampon A is made of cotton; the fibers run crosswise and are compressed into a cylinder one-half inch in diameter and 3 inches long. The tampon is enclosed within two sleeves of stiff glazed paper. The larger sleeve has a diameter of nine-twelfths inch and the smaller, or plunger tube, has a diameter of one-half inch; both are 3 inches long. The tampon is almost completely inserted in one end of the larger sleeve, and the smaller sleeve, or plunger, is inserted in the other end. The larger sleeve is inserted into the vagina, and by pressure on the plunger tube the tampon is pushed into the lumen. A string extends 7 inches from the tampon for aiding in removal. The tampons weigh on an average 3.5 Gm. without the stiff glazed paper sleeves.

Tampon B is made of absorbent wadding formed into a cylinder nine-sixteenths inch in diameter and 2 inches in length. Six loosely braided strings cover and hold the wadding core in shape. A thin layer of cotton covers this cylinder, attached by means of a starch film. This cotton covering is quilted down with sixteen similarly braided fine threads, each securely attached to the cotton covering. The proximal end of the tampon is pressed into a rounded shape to facilitate insertion. A silk thread is securely attached to aid in removal. The tampons weigh on an average 1.8 Gm.

Tampon C has a core of ten circular layers of gauze, 1½ inches in diameter, between two layers of cotton. Each layer of cotton is a thin strip one-half inch wide and wound so as to make a flat roll 1⅝ inches in diameter and one-half inch thick. This forms a sphere of very soft, yielding cotton. A mercerized cotton strip is securely attached and used for removal of the tampon. The average weight is 3 Gm.

Tampons A and C increase in size when placed in fluid in an unconfined space. Tampon B retains its original size under the same conditions.

Our subjects included housewives, clerks, factory workers, laboratory technicians and professional women such as nurses, physicians, artists and business executives; the ages varied from 18 to 46 years. The general plan of our procedure was as follows:

Twelve tampons and an equal number of sanitary pads, individually weighed and numbered, were given to each subject. The time each was worn was recorded on a printed form; the exact time the tampon was inserted and the protective pad was put in place and removed was recorded. As soon as the tampons and pads were removed they were sent to the laboratory. Each tampon and pad was examined and weighed, and

TABLE 2.—*Data on a Subject Who Obtained Complete Protection with Two Types of Tampon and Almost Complete Protection with the Third*

Subject: Factory worker, aged 24, height 5 feet 3 inches (160 cm.), weight 115 pounds (52 Kg.).

Number of Tampon and Pad	Hours Worn	Total Amount Absorbed, Gm.	
		Tampon	Pad
A. Weight of Each Pad 12.3 Gm., Weight of Each Tampon 3.2 Gm.			
1	3:30 p.m. to 9:00 p.m.	6.8	0
2	9:00 p.m. to 5:00 a.m.	3.3	0
3	5:30 a.m. to 1:00 p.m.	5.0	0
4	1:00 p.m. to 7:30 p.m.	5.0	0
5	7:30 p.m. to 5:30 a.m.	4.8	0
6	5:30 a.m. to 4:30 p.m.	4.5	0
7	4:30 p.m. to 5:00 a.m.	5.9 (urine)	0
8	5:00 a.m. to 7:00 p.m.	6.2 (urine)	0
9	7:00 p.m. to 10:30 p.m.	3.4 (urine)	0
Total		44.9	0
B. Weight of Each Pad 11.7 Gm., Weight of Each Tampon 1.7 Gm.			
1	4:00 p.m. to 12:00 p.m.	4.0	0
2	12:00 p.m. to 8:00 a.m.	3.9	0
3	8:00 a.m. to 2:00 p.m.	2.0	0
4	2:00 p.m. to 7:00 p.m.	6.3	0
5	7:00 p.m. to 8:30 a.m.	5.8	0
6	9:00 a.m. to 8:00 p.m.	4.2	0
7	8:00 p.m. to 8:00 a.m.	2.7	0
8	8:00 a.m. to 5:00 p.m.	4.4 (some urine)	0
9	5:00 p.m. to 9:30 a.m.	3.9 (some urine)	0
Total		37.2	0
C. Weight of Each Pad 14.9 Gm., Weight of Each Tampon, 3 Gm.			
1	6:30 p.m. to 11:30 p.m.	9.3 (urine)	0
2	11:30 p.m. to 11:00 a.m.	3.5 (urine)	0
3	11:00 a.m. to 6:30 p.m.	14.0 (urine)	0.5
4	6:30 p.m. to 11:00 p.m.	3.0	0.1
5	11:00 p.m. to 11:00 a.m.	2.5	0
6	11:00 a.m. to 8:00 p.m.	3.0	0
7	8:00 p.m. to 10:30 a.m.	5.0 (urine)	0
Total		42.3	0.6

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the amount of exudate in grams was recorded. We are recording only the objective data obtained from our investigation. It was thought best to exclude the subjective information obtained from questionnaires and from personal interviews conducted by nurses.

Table 1 represents an average normal woman. The amount of catamenial discharge (74.6 Gm.) and the duration of menses (sixty hours) are typical for the age group.

Table 2 A represents a subject who obtained complete sanitary protection by tamponage. Table 2 B shows the same subject using another type of tampon, smaller, but just as efficient. Table 3 illustrates a variation we have frequently observed and can be compared with table 1. Table 4 represents a subject belonging to the heavy-flowing group. We found that one third of our subjects came within this group.

The degree or relative efficiency of the tampons can be summarized briefly by grouping the amounts of catamenial discharge, in grams, absorbed by the protecting sanitary pads; that is, the amounts of exudate which passed the inserted tampons.

TABLE 3.—*Data Illustrating a Frequent Variation*

Subject: Housewife, aged 25, height 5 feet 5 inches (165 cm.), weight 125 pounds (57 Kg.). Weight of each pad 12.4 Gm., weight of each tampon 3.6 Gm.

Number of Tampon and Pad	Hours Worn	Total Amount Absorbed, Gm.	
		Tampon	Pad
1	10:30 p.m. to 6:00 a.m.	8.6	9.6
2	6:00 a.m. to 10:00 a.m.	2.4	1.1
3	10:00 a.m. to 12:00 a.m.	9.6	7.7
4	12:00 a.m. to 9:00 p.m.	4.6	0
5	9:00 p.m. to 7:00 a.m.	8.6 (some urine)	2.2
6	7:00 a.m. to 6:00 p.m.	4.3	0
7	6:00 p.m. to 9:30 p.m.	10.8	0.6
8	9:30 p.m. to 6:00 a.m.	6.0	0.2
9	6:00 a.m. to 4:30 p.m.	10.1 (some urine)	3.4
10	4:30 p.m. to 6:00 a.m.	1.0	0.4
11	6:00 a.m. to 1:00 p.m.	8.2 (mostly urine)	0
12	1:00 p.m. to 6:00 a.m.	0.2	0
Total		74.4 (including urine)	25.2

Tamponage has been advocated and advised for protection during the last part of the period. We found that the protecting sanitary pad was free from exudate during an average of thirty-two hours at the end of the menstrual period of seventy-seven subjects, or 81.1 per cent. Ten subjects (10.5 per cent) could not have used tampons without sanitary pads for the last day of their menstruation. The remaining eight subjects have been mentioned as being able to obtain complete protection throughout their periods by tamponage alone.

Four subjects refused to continue using tampon A after the first one was inserted; the remaining ninety-one subjects used this tampon. All ninety-five subjects used tampon B without complaint. Twenty-one subjects were unable to insert tampon C; hence we have records of only seventy-four complete menstrual periods, for the same number of women. We have records of 260 menstrual periods, for ninety-five subjects; 2,800 tampons were used in these tests.

The examination of the returned tampons in our laboratory indicated that many were saturated with urine. Sixty-five of the ninety-one subjects (72 per cent) who used tampon A, thirty of the ninety-five subjects (32 per cent) who used tampon B and 100 per cent of those who used tampon C showed urine on their recently removed tampons. When the tampon has absorbed hemoglobin to the extent that it has a bloodlike color, it would be necessary to carry out a chemical analysis to ascertain whether urine also is present. We did not do this and hence could determine the presence of urine only by the visual and the olfactory sense in the absence of blood-stained tampons.

TABLE 4.—*Data on a Subject Having a Heavy Flow*

Subject: Nurse, aged 29, height 5 feet 3 inches (160 cm.), weight 135 pounds (61 Kg.). Weight of each pad 11.8 Gm., weight of each tampon 3.3 Gm.

Number of Tampon and Pad	Hours Worn	Total Amount Absorbed, Gm.	
		Tampon	Pad
1	5:00 p.m. to 7:00 p.m.	2.7	0.2
2	7:00 p.m. to 6:00 a.m.	16.7	9.2
3	6:00 a.m. to 9:00 a.m.	13.5	6.6
4	9:00 a.m. to 1:00 p.m.	10.0	0.2
5	1:00 p.m. to 7:00 p.m.	14.7	4.7
6	7:00 p.m. to 6:00 a.m.	14.0	5.4
7	6:00 a.m. to 12:00 a.m.	6.7	0.4
8	12:00 a.m. to 7:00 p.m.	8.2	0.7
9	7:00 p.m. to 7:30 a.m.	1.2	0.2
10	7:30 a.m. to 1:00 p.m.	10.7	2.7
11	1:00 p.m. to 9:00 p.m.	10.7 (small clot)	12.6
12	9:00 p.m. to 6:00 a.m.	1.3	0
13	6:00 a.m. to 9:00 p.m.	4.2 (some urine)	0
14	9:00 p.m. to 6:00 a.m.	1.2	0
15	6:00 a.m. to 4:00 p.m.	1.7	0
16	4:00 p.m. to 6:00 a.m.	2.0	0
Total		119.5	42.9

Blood clots were found adherent to the proximal end of the tampons from eighteen subjects. Questionnaires returned indicated that these eighteen women reported a "gush" of blood immediately after removal of the tampons. This would indicate that the adherent clot had reduced absorbency; hence the tampon acted as a plug, and the catamenial discharge was retained in the vagina proximal to the tampon. The ideal tampon should act as a wick after it has become saturated, so that the exudate will pass downward from the distal end on to the vulva. We found that the tampons with the largest diameter were responsible for the obstruction of the catamenial discharge. Such obstruction occurred only when tamponage was used during the period of heaviest flow. It is obvious that free drainage of the uterine discharge should be maintained during menstruation.

Vaginal tamponage has been a medical procedure, and physicians have kept their patients under observation. Tampons are foreign bodies in the vagina. We do not know from experience how susceptible the vaginal mucosa may be to repeated irritation. When tampons are used regularly during the menstrual period, periodic examination of the vagina should be made to ascertain whether the mucosa remains normal.

TABLE 5.—*Amounts of Exudate Which Passed Through the Tampons*

Grams of Exudate on Protective Sanitary Pads	Number of Subjects	Percentage of Total
None	8	8.4
0.1 to 2.5	26	27.4
2.6 to 5.0	11	11.6
5.1 to 10.0	17	17.9
Over 10.0	33	34.7
	95	100.0

The epithelial cells in the vaginal mucosa are stimulated to cyclic periods of growth by the ovarian hor-

110
938

mones. This cycle of accelerated proliferation may be associated with increased susceptibility to mechanical irritation.

CONCLUSIONS

Ninety-five women, aged from 18 to 46, used self tamponage for catamenial sanitary protection. Each wore a sanitary pad and returned both tampon and protecting pad for examination. Eight women did not need the protecting pad, since tampons afforded complete protection. Eighty-seven (91.6 per cent) needed more protection than was provided by any of the three types of tampons used. Seventy-seven (81.1 per cent) women could have used tampons alone during the last part of their period.

PRIMARY OBLITERATIVE PULMONARY ARTERIOLAR SCLEROSIS

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My purpose in this report is to present the unusual anatomic manifestations of obliterating arteriolar sclerosis of the pulmonary vessels in the absence of significant sclerosis of the systemic vessels.

Atheromatous change in the pulmonary vessels occurs frequently in persons affected by a generalized arteriosclerosis. The presence of atheromatous plaques in the larger pulmonary vessels without marked systemic arteriosclerosis likewise is fairly common. However, such pathologic change can scarcely be considered significant. Almost invariably when pulmonary arteriosclerosis is capable of causing symptoms, it exists as arteriolar sclerosis, and it may be assumed that the significant vascular lesions referred to by writers describing the disabilities of patients involve the arterioles. In a series of more than 3,800 autopsies at the New Haven Hospital, the present case is the only one of its kind. The infrequence of the anatomic picture is attested by MacCallum [1] in a report of a similar case, the only one in a series of 12,000 autopsies at Johns Hopkins Hospital.

Pulmonary arteriosclerosis has had a tradition in the Argentine school of medicine since the clinical lecture in 1901 of Dr. Abel Ayerza, professor of medicine in the National University of Buenos Aires. He described a case of cardiac failure showing such a degree of cyanosis as to suggest the term "cardiac negro." Since then the term "Ayerza's disease" has been employed by many authors. The development of the theme has been carried out chiefly by the Argentine school and especially by two of Ayerza's pupils, Arrillaga [2] and Escudero.[3] A review of the French and South American literature on this subject makes clear the controversial nature of this rather nationalized nomenclature and explains the confusion attending the definition of the term "Ayerza's disease." To most people it means cardiac failure associated with pulmonary arteriosclerosis, and with the absence of any significant systemic vascular changes.

As a matter of fact, in the autopsy of Ayerza's patient the pulmonary vessels were not remarkable but dilatation of the bronchi, peribronchitis and hypertrophy and dilatation of the right side of the heart were described. Escudero in 1905 found a case that showed similar symptoms and signs and marked pulmonary atherosclerosis. In 1908 Rogers [4] reported ten cases of primary sclerosis of the pulmonary vessels and concluded that syphilis was a likely cause. In 1909 C. A. Marty first used the term Ayerza's disease in a published document. Since then there has been considerable dissension between Ayerza's two most interested pupils, Arrillaga and Escudero. The former has come to the view that Ayerza's disease is primarily a syphilitic pulmonary arteritis, often complicated by mitral stenosis or chronic bronchitis. Escudero considers Ayerza's disease to mean a syphilitic bronchitis in which chronicity is associated with a secondary arteriosclerosis attendant on general loss of elasticity and fibrosis of the lung. He divides the typical case into two phases, (1) the "bronchial period," in which the signs are bronchial, often mild, and accompanied by a moderate polycythemia, and (2) a cardiac phase, itself further divided into two parts, a period of compensation and one of decompensation in which the aspect of the black cardiac finally arrives. Congenital but not acquired syphilis, according to Escudero, is able to effect this picture.

Warthin [5] believed that Ayerza's disease was due to syphilis and presented a case in 1917 in which Spirochaeta pallida was demonstrated in the walls of the sclerosed pulmonary vessels. Clinically, however, the resemblance to the case described by Ayerza was slight. Naturally, the frequent presence in the lung of spirochetes other than Spirochaeta pallida removes the importance of such demonstrations.

There is a considerable body of French literature on the subject. Most French authors feel that the sclerosis in the pulmonary vessels is secondary to long-standing chronic bronchitis and emphysema. The conclusions of French writers are well summed up by Legrand.[6] He states that the "black cardiac" refers to a syndrome of progressive obliteration of the pulmonary artery and its branches and that it varies in cause in different cases.

In sifting the matter down, one must come to the conclusion that the term "Ayerza's disease" rests on an insecure footing. In spite of the descriptive quality of the term "black cardiac," chronic cyanosis is hardly limited to cases of sclerosis of the pulmonary vessels. The name "Ayerza's disease" is exceedingly dear to the Argentine school, but it would seem more logical to label cases showing obliterating sclerosis of the pulmonary arterioles without evidence of systemic sclerosis and without evidence of significant antecedent pulmonary disease as "primary obliterative pulmonary arteriolar sclerosis."

To be classified as such, a case should display at the most only insignificant systemic atherosclerosis and no hypertrophy of the left side of the heart. Mild emphysema, slight collections of small round cells and slight fibrosis of the bronchial walls must be expected as

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V 1
193

secondary to the vascular change. After the full course of the disease with attendant cardiac failure complicated by terminal focal pneumonia, the primary nature of the arteriolar sclerosis may be masked and it is doubtful whether syphilis can be demonstrated as the cause. Cases of secondary pulmonary arteriosclerosis are less infrequent and more often than otherwise are secondary to long-standing chronic infection of the bronchial tree.

The symptoms and signs coincident with gradual obliteration of the pulmonary vessels follow a perfectly logical sequence and have been described. The inability of the alveoli to aerate sufficient quantities of blood per time unit leads to compensatory emphysema and polycythemia. The increase of pulmonary vascular resistance leads to the eccentric hypertrophy of the right heart. Cyanosis is naturally marked and continuous. The usual signs of cardiac failure appear when the myocardium is pushed beyond its reserve.

The case to be presented fulfils the requirements suggested for the category of primary obliterative pulmonary arteriolar sclerosis.

REPORT OF CASE

History.—A white woman, aged 68, American, a housewife, entered the New Haven Hospital Aug. 19, 1935, complaining of cough, shortness of breath and swelling of the legs of a month's duration. Her family history was irrelevant. No history of respiratory or vascular disease was elicited. No record of exposure to dusty environment was obtained. The patient felt well until a month before entry when she became aware of the gradual onset of dyspnea and cough. This was soon followed by swelling of the legs. These symptoms were progressive in severity. Fatigue became prominent. She became orthopneic and was troubled by vague indigestion and gaseous distention. Her weight increased from 118 to 132 pounds (from 53.5 to 60 Kg.) despite her poor appetite. The swelling of her legs ascended over the abdominal wall. She was treated by her family physician with digitalis, with some relief of dyspnea. The patient did not have the advantage of rest during her illness and continued to carry out her rather strenuous household duties.

Examination.—The patient's general appearance did not suggest acute illness. The temperature was 99.8 F., the pulse 100 and the respiratory rate 26. The blood pressure was 160 systolic, 110 diastolic. She appeared orthopneic and markedly cyanotic. The neck veins were distended. The heart was thought to be enlarged to the left. At the apex a loud rough murmur extended through systole. The sounds at the base were faint with a distinct gallop rhythm and occasional dropped beats. The electrocardiogram indicated interventricular block and right ventricular preponderance. The lungs were clear save over both bases posteriorly, where resonance and fremitus were impaired and many moist râles were heard. Edema of the abdominal wall and extremities was present. Ascites was not made out. Beyond this, no unusual physical appearances were present.

Treatment and Course.—The patient was placed in bed and given digitalis, but fluid rapidly accumulated at the right base. Thoracentesis was considered but it was thought best to temporize for another twenty-four hours. However, early in the morning of the third day she grew restless, then extremely weak, and suddenly ceased breathing.

Her admission blood count disclosed a hemoglobin of 91 per cent (Tallqvist), a red cell count of 6,200,000 and a white count of 5,500. The differential white count revealed 78 per cent polymorphonuclears, 19 per cent lymphocytes, 2 per cent large monocytes and 1 per cent basophils. The smear was not remarkable. The Wassermann reaction was negative. Urinalysis recorded a cloudy yellow uncatheterized specimen with an acid reaction, a 2 + albumin and no sugar. The quantity was insufficient for specific gravity determination and the sediment contained from 30 to 40 white cells per high power field.

Autopsy.—Only the essential facts will be given from the complete protocol. These concern the heart, lungs and vascular system.

The lungs were small and collapsed. Pleural adhesions were not present. The right pleural cavity contained 300 cc. of serosanguineous fluid and the left pleural cavity 150 cc. The pericardium was distended with clear straw-colored fluid. There were no pericardial adhesions. The transverse diameter of the heart was 13 cm. and the chest 21 cm. The pulmonary artery was opened in situ with the release of only fluid blood.

The heart weighed 390 Gm. The epicardium was shining and transparent. The subepicardial fat was not increased and through it coursed patent coronary vessels. When the heart was opened a marked eccentric hypertrophy and dilatation was found limited entirely to the right ventricle. The myocardium presented a homogeneous reddish brown cut surface without the presence of fibrous scars or fresh infarct. The endocardium was smooth, shining and transparent throughout. The columnae carneae of the right ventricle were flattened but well rounded in the left. The chordae tendineae were thin and delicate and attached beyond the free border to the lower surface of thin velamentous valve leaflets. The aortic and pulmonic cusps appeared intact and competent, approximating in a neat line of closure. The right ventricle wall measured 9 mm. in thickness and the left 11 mm. The tricuspid, pulmonic, mitral and aortic valves measured respectively 11.5, 5, 8.5 and 7 cm. No antemortem thrombi were found. No developmental anomalies were present.

The right lung weighed 200 Gm. It was small and collapsed. A mottled pink and gray parenchyma shone through a uniformly smooth and transparent pleura. The lung was everywhere finely crepitant and no discrete areas of increased density were palpable. At the borders of the lobes were raised patches of emphysematous lobules. The cut surface showed a homogeneous, finely granular, mildly crepitant gray surface. No exudate exuded from the cut surface, which appeared curiously dry in spite of the pleural transudate. The vessels were markedly sclerosed and were studded with atheromatous plaques. The larger branches were somewhat dilated and strangely immovable, as though blocked by obstruction farther ahead in the arterioles. Smaller branches from 1 to 2 mm. in diameter stood out from the cut section in a stiff bas relief. The bronchial branches were free from exudate or obstructive lesions. The bronchial mucosa was smooth and shining. No enlarged lymph nodes were present at the hilus. No unusual pigmentation was noted.

The left lung weighed 170 Gm. and was exactly similar to the right lung, as were its hilar structures.

The aorta, together with its larger branches, was an elastic, even calibered vessel with a very few small atheromatous plaques on the otherwise perfectly smooth intima.

On microscopic examination of the heart the epicardium was thin. The myocardial fibers were well preserved and stained. The individual fibers of the right myocardium were visibly larger than those of the left. No replacement fibrosis was seen. No cellular leukocytic infiltrations were present. The coronary vessels displayed no significant sclerosis. The endocardium was thin and reactionless.

Sections of the lung revealed a uniformly thin pleura. There was a mixed emphysema and atelectasis. The alveolar walls were mildly thickened by fibrosis. The alveolar spaces were uniformly free of exudate, save for rare small collections of lymphocytes and monocytes. Pigment was never present in unusual amount. The larger vessels presented atheromatous changes in the intima, with moderate fibrosis of the media. In the arterioles the lumens were reduced in size by this change at times to complete occlusion. Lifting up and reduplication of the intimal layer and a dense fibrosis of the media were present. In some arterioles there was evidence of canalization of old well organized thrombi. There was, however, no inflammatory reaction anywhere, acute or chronic. The picture on the whole was reminiscent of renal arteriolar sclerosis.

Sections of the aorta revealed a slight thickening in the intima with some hyalinization. No granulation tissue was present in the media, which for the most part supported unbroken elastic fibers. No perivascular leukocytic infiltrations

110
938

were found. It is to be emphasized that arteriolar changes such as described in the lung were found in no other tissue.

The anatomic diagnosis was written: Primary: Primary obliterative pulmonary arteriolar sclerosis; hypertrophy and dilatation of right side of the heart; chronic passive congestion of viscera; anasarca with hydropericardium; hydrothorax (bilateral) and ascites; pulmonary atelectasis and emphysema. Subsidiary: Diverticulitis of sigmoid colon; cervical polyp; hallux valgus (bilateral); fetal adenoma of thyroid.

REFRACTORY ANEMIA

ANALYSIS OF ONE HUNDRED CASES

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The recent development of a clearer understanding of pernicious anemia and of the conditions which are allied to it has made more prominent the anemic states which do not respond to adequate therapy with liver extract or with iron. These refractory anemias have been long recognized but have been classified loosely as severe secondary, aregenerative or aplastic anemia. Insufficient information has been available, however, to warrant any conclusions concerning the fundamental nature of the conditions. For this reason, a clinical and experimental study of refractory anemia has been made at the Hospital of the Rockefeller Institute. In the series, all those patients have been included who were referred to the institution with anemia of severe degree which did not respond to the usual therapeutic methods. In this way a suitable cross section of the problem as it presents itself to the practitioner was obtained.

The diagnosis of refractory anemia can be made only rarely on hematologic evidence alone. Anemia is moderate to most severe, slight macrocytosis is a feature and the shape of the red cells may deviate only slightly from the normal or may show the most profound alterations. Leukopenia is almost always present and may be mild or extreme; it is usually associated with granulopenia and with the presence of abnormal, so-called toxic polymorphonuclear cells. Thrombopenia is usually marked but may be absent. Refractory anemia may frequently be differentiated from other anemic states by the prominence of hemorrhagic phenomena and by a tendency to the development of necrotic lesions of the mucous membranes. Fever is frequent and may be a prominent feature.

The cases of refractory anemia may be divided into two general groups, those in which the anemia is associated with a recognized disease entity and is presumably secondary, and those in which it seems to occur independently. The secondary type is included because frequently it cannot be recognized from the hematologic data alone and hence it may be a serious problem in differential diagnosis. Of the forty patients with secondary refractory anemia ten had Hodgkin's disease involving the bone marrow, four had obscure malignant neoplasms, twelve had presumptive evidence of degenerative disease of the liver, one had tuberculosis of the bone marrow and thirteen had either lymphoid or myeloid aleukemic leukemia. In many instances conclusive evidence of the primary disease process was obtained only from the histologic study of sternal bone marrow removed at biopsy.

Sixty cases of apparently primary refractory anemia were studied and divided into four groups on the basis of the pathologic changes of the bone marrow as seen at biopsy, at autopsy or both. The four basic pathologic changes were sclerosis, normal cell hyperplasia, immature cell hyperplasia and immature cell hypoplasia. Sclerosis of the marrow was present in three cases. In twelve, an active marrow with apparently normal maturation was present, and in eight of these the presence of a hemolytic process was confirmed by studies of urobilin output. Studies of pigment excretion were not made in the remaining four cases. Hyperplastic, cellular marrows, infiltrated densely with uniformly immature cells, were present in eighteen cases. The cells were so undifferentiated that their nature could not be determined absolutely. This condition has been described by Thompson, Richter and Edsall[1] and is considered by some observers to be aleukemic leukemia. The absence of a leukemic blood picture, of leukemic tumor and of leukemic infiltration of organs is the basis for considering the group to be an independent one. The remaining twenty-seven cases were marked by hypoplasia to almost total aplasia of the marrow structure. This group differed from the one with hyperplastic marrow only in cellularity, since the predominant type is a similar primitive, immature cell. When considered physiologically the condition is the result of disturbance of cell destruction or cell maturation or of both factors. Considerable information is afforded by studies of pigment excretion as an index of cell destruction and of coproporphyrin-I excretion as a measure of marrow activity.

The etiology of refractory anemia is obscure, but certain suggestions deserve consideration. The basic lesion of the bone marrow in the types marked by decrease of cell production with a predominance of primitive cell elements is very like that seen in acute granulopenia, a condition in which an abnormal susceptibility to certain chemical compounds has been established as etiologic in certain instances. Some evidence is at hand which suggests that a similar process if continued sufficiently long may be operative in causing a disturbance of erythropoiesis as well as of myelopoiesis.

Analysis of sixty cases of primary refractory anemia gives a history of exposure to compounds which may be toxic to the hemopoietic system in twenty-seven cases, or 45 per cent. This number is considered to be significant in view of the limited knowledge of the various factors which give rise to drug hypersusceptibility.

No suggestive toxic agent could be established for the group with sclerotic marrow. Two patients with hemolytic anemia and hyperplastic, normal cell marrow had been exposed to benzene and two had been given arsphenamine. One patient with active marrow for whom no pigment studies are available was proved to be sensitive to aminopyrine. Of the patients with hyperplastic immature cell marrow, two had radium poisoning, two had used aminopyrine, one was exposed to a number of potentially toxic solvents in his work as a roofer, two had been exposed to benzene, two had used a potentially toxic hair dye for many years and one had used cresote medicinally. Of the patients with

From the Hospital of the Rockefeller Institute for Medical Research.
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1. Thompson, W. P.; Richter, M. N., and Edsall, K. S.: Am. J. M. Sc. **187**: 77 (Jan.) 1934.

hypoplastic immature cell marrow, four had been exposed to benzene, two to arsphenamine, one to cinchophen, two to aminopyrine, one to acetophenetidin, one to hydroquinone, one to possibly toxic solvents in his work as a printer, two to excessive amounts of a naphthene-containing insecticide, one to creosote and one to a potentially toxic hair dye. It should be emphasized that in most instances the exposure to possibly toxic chemicals was no greater than most persons can tolerate without difficulty.

The outcome of refractory anemia is not necessarily fatal, although it may well be so. For secondary anemia the prognosis is that of the primary disease. Of the sixty patients with primary anemia, seventeen had a well defined remission at some time. Of the seventeen remissions, fourteen were complete and three were only partial. Of all the remissions, six continued as long as the patients were observed, but in the remainder of the patients the disease recurred and terminated fatally.

Any discussion of the therapy of refractory anemia must be largely negative. Stomach preparations, whole liver and liver extract given in maximum dosage by both oral and parenteral routes have uniformly failed. No iron preparation has had any effect. Vitamin C has failed not only to alter the course of the disease but also to control the hemorrhagic phenomena. Transfusion has never had more than a transient effect on the course of the disease but may carry the patient along until the marrow function has recovered spontaneously. Some evidence is at hand that, for carefully selected patients with ample functioning bone marrow, an elevated reticulocyte level and evidence of definitely increased hemolysis, splenectomy may be a useful procedure. The nucleic acid derivatives have been uniformly without effect.

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SUMMARY AND CONCLUSIONS

Analysis of 100 cases of refractory anemia proves the existence of two major groups, those of primary and those of secondary anemia, in which the condition cannot always be differentiated on hematologic evidence. The cases of primary anemia may be subdivided on pathologic grounds into four groups, based on the presence of sclerotic, normally hyperplastic, immature hyperplastic or immature hypoplastic marrow. The physiologic mechanism is a disturbance of cell production or of cell destruction or both. When cell production is interfered with, the basic lesion is a predominance of primitive cell elements. In 45 per cent of the cases of primary anemia, a history of exposure to chemical compounds which may be hematologically toxic was present. Temporary remissions occurred in 25 per cent and permanent remissions in 6 per cent. No treatment was effective.

Sixty-Sixth Street and York Avenue.

ABSTRACT OF DISCUSSION

DR. GEORGE R. MINOT, Boston: The fact that the authors have been enabled to study during the last few years a hundred cases of relatively rare conditions leading to anemia, of a type for which no significant treatment exists, illustrates the value of institutions for clinical investigation. Their excellent work has been dependent on their diligence and on the foresight of individuals to place at their disposal the means for good work. It is also dependent on the cooperation of physicians and the patients themselves, for they have given him the opportunity to study cases. Drs. Rhoads and Barker have emphasized the importance of realizing that these patients often have a macrocytic blood picture which is easy to confuse with that of pernicious anemia. The red cells do not vary as much in size as they usually do in pernicious anemia for a given red cell level. The cases tend to be diagnosed as pernicious anemia which has not responded to liver therapy. There is no evidence that the condition is due to an inability to use liver extract. Unlike pernicious anemia, the occurrence of a sore tongue is at least rare and achlorhydria is often not present. The patients are much less apt than those with pernicious anemia to be blue eyed and to have premature gray hair. The classic type of aplastic anemia, in which the marrow is like butter, which usually occurs in young women and runs a rapidly fatal course over two or three months, is distinctly rare. It is more common now to recognize the cases of long duration, of a year at least and often, as Dr. Rhoads has pointed out, of several years' duration. Some such patients have been kept alive by means of more than a hundred blood transfusions. In such cases, rarely large doses of liver extract cause a relatively slight reticulocyte response and increase of red cells, which usually do not occur again with repetition of liver therapy as anemia increases. As to some of the secondary types: Hodgkin's disease of the bone marrow is occasionally seen with pronounced increases of reticulocytes and sometimes there is slight increased fragility of the red cells to hypotonic salt solution. One theoretically ought to be able to tell the secondary types. One may do so in many instances, but unfortunately too often a precise diagnosis cannot be made until biopsy or autopsy. A confusing situation is as follows: Rarely a patient who has undoubted leukemia with a classic blood picture has some weeks before death leukopenia with rapid progression of anemia and at autopsy the bone marrow is fatty and the pathologist is unable to find definite evidence of leukemia. A comparable condition may occur in the hemolytic anemia arising from trinitrotoluene poisoning. Usually in such cases the marrow is actively regenerating, but rarely the cases may terminate with a fatty marrow.

DR. RANDOLPH WEST, New York: In dealing with bone marrow, which is a complex organ with many cell types, there tends to be a certain amount of added difficulty because of the complexity of histologic structure. If one thinks of bone marrow as a simple tissue, as one might think of an ordinary gland, and then considers the possible types of response to a given injury, I think that many of the aplastic anemias will fall into a grouping that may be profitable to think about. If a destructive agent is present in the blood in sufficient concentration, there may be complete obliteration of the marrow, with a resulting fatty marrow, which was the one described by all the earlier workers in aplastic anemia. If the agent is present in smaller amounts it is possible that repair may take place after the agent has ceased to act, and the pattern of repair may lead to practically normal regeneration of functionally adequate marrow. If the pattern of repair is somewhat different, for reasons that are not yet understood, there may be the analogue of what in a glandular structure would be called an adenoma; in other words, the appearance of large amounts of anatomically fairly good looking but functionally imperfect tissue. It seems to me that the aplastic anemias with hyperplastic bone marrow may well fall into this group. One step beyond that: The type of regeneration may not be the analogue of a benign adenoma but may approach the type of true malignant disease. In this group probably fall aleukemic leukemias and the true leukemias. I think that, while therapeutic measures applied after the pattern of a cell regeneration has been determined by various unknown factors in the body give little hope of successful therapeutic results, the application of these measures during the earliest stages of regeneration after injury may well determine the pattern of regeneration. Certainly in the early benzene poisoning cases, and also in the early aplastic anemias, one gets the clinical impression that a very adequate food supply to the bone marrow, chiefly liver extract and iron, may be of use in certain instances.

DR. HYMAN I. GOLDSTEIN, Camden, N. J.: In Vienna I spoke to Prof. Julius Bauer concerning anemias that failed to respond to the ordinary liver preparations and asked whether he had tried intra-ossal injections of highly concentrated liver extract, through Arinkin puncture or trephine, as suggested

originally by Arnold Josefson of Stockholm, who gave liver extract intrasternally and treated about twenty-five patients with this method (1930-1934). On the advice of Julius Bauer I have used a highly concentrated liver extract in a few instances. In some resistant cases of the types of anemia mentioned by the authors highly concentrated preparations, with the joint use, perhaps, of large doses of iron and spleen extract (by injections and orally), with or without blood transfusions, may give better results. Also, in cases of pernicious anemia in which there is allergy to liver or complicating arthritis perhaps the use of carefully prepared spleen and brain and kidney tissue extract with large doses of iron and blood transfusions may be helpful and life saving. William Schlesinger of Vienna informed me of his experience with concentrated spleen extract, in such cases. Spleen extract of high concentration and almost free of foreign protein material, by injections, is helpful in relieving itching skin conditions and weeping eczemas, which may at times occur as complications of severe anemias, jaundice, leukemias and Hodgkin's disease.

DR. C. P. RHOADS, New York: Dr. Minot called our attention to something we had left out of the talk which we had planned. Symptomatically it is quite true that one can make a good clinical guess that one is dealing with a case of refractory anemia. It is not universal, glossitis of marked degree is rare, and neurologic disturbance is exceedingly uncommon, if not absent. Unfortunately, there were in the group examples in which there was glossitis. Of course, stomatitis is very common and very severe. There were just enough who had confusing symptoms in the central nervous system so that I, at least, cannot be perfectly certain until I have given therapeutic tests of liver extract. Splenectomy is a difficult question. We find it is rather entered into hastily in this type of case. We do believe that a very small group exists in which there is relatively good activity of the marrow, rather good maturation of cells in the marrow. We have endeavored to pick out cases in which splenectomy might be a life saving procedure. We have seen only three such cases, and we have removed the spleen in quite a number of other cases simply on the chance that we might pull some one out of a very bad situation. I think the operation can be used. I think it must be used with the greatest care and with every diagnostic aid employed before such a radical procedure is entered on. As to the question of disease of the bone marrow, of course that is a very moot point. I think it requires great experience to evaluate properly the histologic picture of the bone marrow. We have been deceived, and are still being deceived. It will tell, however, whether one has encountered an obscure case of pernicious anemia. I think it is a useful procedure both from the diagnostic point of view and from the point of view of classification and of understanding this difficult and distinctly obscure group of conditions.

Sympathin and Parasympathin.—The mode of response of autonomic nerve stimulation is correlated with the properties of the chemical mediator liberated as a result of such stimulation. The chemical mediator commonly liberated by sympathetic stimulation possesses properties of adrenin and has been called sympathin; the one commonly liberated by parasympathetic stimulation possesses properties of acetylcholine and has been called parasympathin. Fibers whose stimulation results in the liberation of an adrenin-like mediator consequently may be called adrenergic, and those whose stimulation results in the liberation of an acetylcholine-like mediator, cholinergic. The fibers of sympathetic and parasympathetic origin are not mutually exclusive with regard to the chemical mediators. For example, stimulation of the sympathetic fibers which mediate constriction of the peripheral blood vessels results in the liberation of sympathin, while stimulation of those which mediate dilatation of the peripheral blood vessels results in the liberation of a chemical mediator with the properties of parasympathin. The responses elicited by stimulation of the latter fibers obviously belong to the same category as those elicited by stimulation of parasympathetic nerves.—Kuntz, Albert: Relation of Autonomic Nervous System to Physical Therapy, *Arch. Phys. Therapy* **19**:24 (Jan.) 1938.

PHENOLPHTHALEIN STUDIES

ELIMINATION OF PHENOLPHTHALEIN

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The discoverer of the cathartic action of phenolphthalein, Zoltan von Vamossy,[1] determined that more than 85 per cent of ingested phenolphthalein is eliminated in the dog's feces and that merely a minimal quantity of free phenolphthalein is occasionally to be found in the urine on the addition of alkali. He also noted in dogs, after the giving of enormous doses, an increase in the conjugated sulfates in the urine.[2]

Kastle probably was the first to discover the presence of conjugated phenolphthalein in the urine. After giving a dose of 0.5 Gm. of phenolphthalein intraperitoneally to a guinea pig he observed the excretion of conjugated phenolphthalein in the urine for twenty days.

Fleig[3] studied exhaustively the fate of phenolphthalein in the system, and he as well as others concluded that phenolphthalein is so stable a compound that it is not decomposed into phenol and phthalic acid in the system. When given by mouth in large doses it passes in the free state into the urine, where it can be discovered by the addition of sodium hydroxide; it also causes an increase in the quantity of conjugated sulfates in the urine. This increase of the conjugated sulfates is particularly marked in animals that received injections of it under the skin or into the blood. A relatively small portion of conjugated glycuronate was also found in the urine of dogs after ingestion of large doses of phenolphthalein.

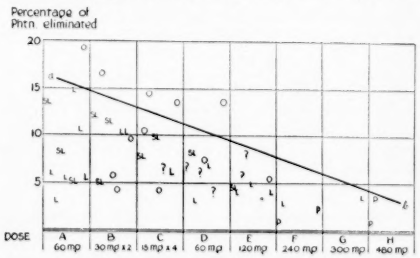

Chart 1.—Elimination of phenolphthalein in relation to dose and to cathartic action. The line *a-b* indicates that the larger the dose the smaller the percentage of phenolphthalein eliminated, obviously because the greater the cathartic action the less the percentage of phenolphthalein absorbed.

We have found in a previous study of urinary elimination following 1,000 medicinal doses of phenolphthalein[4] that, after small medicinal doses, free phenolphthalein is usually absent from the urine and that the larger the dose the more frequently does free phenolphthalein appear in the urine. Conjugated

From the Laboratory of Pharmacology and Therapeutics, University of Illinois College of Medicine.

1. von Vamossy, Zoltan: Ueber ein neues Abführmittel (Purgen) Therapie der Gegenwart, München. med. Wchnschr., May 1902.
2. von Vamossy, Zoltan: Ist "Purgen" ein schädliches Abführmittel? München. med. Wchnschr. **50**: 11-24 (June 30) 1903.
3. Fleig, M. C.: Deux purgatifs synthétiques, Arch. int. **18**: 327-371, 1908.
4. Fantus, Bernard, and Dyniewicz, J. M.: Phenolphthalein Studies: 1,000 Doses of Phenolphthalein: Urinalyses, J. A. M. A. **108**: 439-443 (Feb. 6) 1937; IV. Phenolphthalein Solubilities, Am. J. Digest. Dis. & Nutrition **3**: 573-577 (Oct.) 1936.

phenolphthalein, on the other hand, is always present, so that testing for conjugated phenolphthalein may serve as a test that phenolphthalein has been ingested. The estimation of the quantity of free and of conjugated phenolphthalein in the urine may serve as a measure of the elimination of total phenolphthalein in the urine.

Since, in the previous study, we had the opportunity of assaying but a single twenty-four hour specimen of urine after a dose of phenolphthalein, which gave us the qualitative data recorded, it seemed desirable to make careful quantitative estimations of the total amount of phenolphthalein eliminated in the urine after a medicinal dose by continuing the determinations of the quantity contained in successive twenty-four hour specimens until it was no longer found in the urine. This may give a basis for the determination of abnormalities of elimination, as well as a means for the evaluation of methods of treatment after phenolphthalein overdosage.

METHOD OF STUDY

The urine specimens were obtained from volunteers, chiefly young medical students, who furnished a portion of the mixed twenty-four hour collection, preserved by xylene, and a statement of the total quantity of urine passed. This was continued on consecutive days after taking a specified dose of white phenolphthalein at bedtime until the urine was found free from phenolphthalein. The following doses were administered at intervals of a week and will be referred to for the sake of brevity under the letters given:

Dose A: White phenolphthalein, 0.06 Gm. in capsule, taken at bedtime.

Dose B: White phenolphthalein, 0.03 Gm. in two capsules, one at bedtime and one in the morning.

Dose C: White phenolphthalein, 0.015 Gm. in four capsules, one at bedtime, one in the morning, one four hours later, and one four hours after this.

Dose D: White phenolphthalein, 0.06 Gm. in capsule, taken at bedtime (as control for dose A).

Dose E: White phenolphthalein, 0.12 Gm. in capsule, taken at bedtime.

Dose F: White phenolphthalein, 0.24 Gm. in capsule, taken at bedtime.

Dose G: White phenolphthalein, 0.30 Gm. in capsule, taken at bedtime.

Dose H: White phenolphthalein, 0.48 Gm. in capsule, taken at bedtime.

The analyses were conducted as follows:

Method of Determining Conjugated Phenolphthalein in Urine.—Heat 10 cc. of urine and 10 cc. of 10 per cent hydrochloric acid on a water bath for from three to four hours to break up the conjugation. Allow the solution to cool. Extract with ether in from 15 to 20 cc. portions until a small volume of the last washing shows no trace of phenolphthalein when tested with sodium hydroxide volumetric solution.

The combined, filtered ether portions containing the freed phenolphthalein are shaken with a small portion of tenth normal sodium hydroxide volumetric solution and allowed to stand until the mixture has completely separated. The alkaline solution is then drawn off into a second separator and the process repeated until all the phenolphthalein is extracted. The combined alkaline solutions are then made acid with the smallest amount of hydrochloric acid and again extracted with ether.

The ether portions are made alkaline with tenth normal sodium hydroxide volumetric solution (the volume used depending on the amount of phenolphthalein present) and compared with the same volume of tenth normal sodium hydroxide volumetric solution, to which is added a known standard phenolphthalein solution to color equality, and the amount of phenolphthalein present is calculated.

Method of Determining Free Phenolphthalein in Urine.—Extract 10 cc. of urine with ether in from 15 to 20 cc. portions until a small volume of the last washing shows no trace of phenolphthalein when tested with tenth normal sodium hydroxide volumetric solution. The combined, filtered ether portions containing the phenolphthalein are shaken with tenth normal sodium hydroxide volumetric solution, the volume used depending on the amount of phenolphthalein present. It is advisable to make the extraction with as few separations as possible and to make the reading quickly, because phenolphthalein in alkaline solution tends to decolorize. This solution is compared with the same volume of tenth normal sodium hydroxide volumetric solution, to which

Report of Cases

Dose	Laxative Action*	Conjugated Phenolphthalein Eliminated	Percentage of Dose	Free Phenolphthalein Eliminated	Percentage of Dose
Case 1, R. F.					
A. 60 mg.	SL	8.3 mg.	13.8	0	0
B. 30 mg. × 2	SL	7.4 mg.	12.4	0	0
C. 15 mg. × 4	SL	4.83 mg.	8.0	0	0
D. 60 mg.	O	4.015 mg.	6.7	0.27 mg.	0.45
E. 120 mg.	SL	5.75 mg.	4.8	0	0
F. 240 mg.	P	2.8 mg.	1.16	0.1 mg.	0.04
H. 480 mg.	P	4.9 mg.	1.02	1.005 mg.	0.21
Case 2, M. H.					
A. 60 mg.	L	3.65 mg.	6.1	0.13 mg.	0.216
B. 30 mg. × 2	SL	3.08 mg.	5.13	0	0
C. 15 mg. × 2	O	6.62 mg.	11.3	0.3325 mg.	0.554
D. 60 mg.	SL	5.2 mg.	8.61	0.105 mg.	0.175
E. 120 mg.	L	5.53 mg.	4.6	0	0
F. 240 mg.	L	7.085 mg.	2.95	0.325 mg.	0.22
H. 480 mg.	P	15.33 mg.	3.2	2.32 mg.	0.483
Case 3, E. F.					
A. 60 mg.	L	2.06 mg.	3.43	0.18 mg.	0.3
B. 30 mg. × 2	O	10.0 mg.	16.6	0	0
C. 15 mg. × 4	O	8.8 mg.	14.6	0.296 mg.	0.49
D. 60 mg.	L	2.02 mg.	3.36	0	0
E. 120 mg. (*a*)	?	6.44 mg.	5.36	1.278 mg.	1.06
60 mg. (*b*)	?	4.73 mg.	3.94	0.994 mg.	0.829
Case 4, I. I.					
A. 60 mg.	SL	4.9 mg.	8.11	0.19 mg.	0.31
B. 30 mg. × 2	SL	6.985 mg.	11.6	0	0
C. 15 mg. × 4	SL	5.9 mg.	9.83	0	0
D. 60 mg.	?	3.9 mg.	6.6	0.086 mg.	0.143
E. 120 mg.	?	4.99 mg.	4.15	0.12 mg.	0.1
Case 5, E. S.					
A. 60 mg.	L	3.4 mg.	5.6	0	0
B. 30 mg. × 2	O	3.676 mg.	6.01	0.098 mg.	0.16
C. 15 mg. × 4	O	2.623 mg.	4.37	0	0
D. 60 mg.	O	4.6 mg.	7.66	0	0
E. 120 mg.	L	5.99 mg.	4.99	0	0
Case 6, J. S.					
A. 60 mg.	SL	3.265 mg.	5.4	0	0
B. 30 mg. × 2	O	2.605 mg.	4.35	0	0
C. 15 mg. × 4	?	4.21 mg.	7.01	0	0
D. 60 mg.	L	4.24 mg.	7.0	0	0
Case 7, G. M.					
A. 60 mg.	L	9.04 mg.	15.1	0	0
B. 30 mg. × 2	L	6.33 mg.	10.55	0	0
C. 15 mg. × 4	L	3.85 mg.	6.4	0	0
D. 60 mg.	?	2.8 mg.	4.67	0	0
Case 8, R. L.					
A. 60 mg.	L (3d day)	6.285 mg.	10.47	0.125 mg.	0.21
B. 30 mg. × 2	L (3d day)	6.2175 mg.	10.3	0.3225 mg.	0.537
Case 9, W. T.					
A. 60 mg.	O	11.703 mg.	19.5	0.123 mg.	0.205
B. 30 mg. × 2	O	5.903 mg.	9.8	0	0
C. 15 mg. × 4	O	8.36 mg.	13.9	0	0
D. 60 mg.	O	8.3 mg.	13.8	0	0
E. 120 mg.	O	6.775 mg.	5.65	0	0
H. 300 mg.	L	10.01 mg.	3.0	1.25 mg.	0.417
Case 10, C. M.					
A. 60 mg.	L	2.5 mg.	4.16	0.784 mg.	1.3
E. 120 mg.	L	4.56 mg.	3.8	0.445 mg.	0.37
F. 240 mg.	P	7.45 mg.	3.1	0.48 mg.	0.20

* The symbols used here and in chart 1 are as follows: O indicates no cathartic action; ?, no report; SL, slight laxative action; L, laxative action—soft stool; P, purgative action—liquid stool.

is added a known standard phenolphthalein solution to color equality, and the amount calculated.

We are able to report on the results secured as to total elimination after the taking of fifty-five doses by ten different volunteers who were thoroughly cooperative, as shown in the accompanying table. We also have results of the single twenty-four hour elimination after 1,000 doses of phenolphthalein. It seems that this can best be done in the form of graphs.

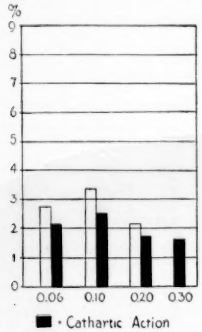

Chart 2.—Average percentage of the dose of phenolphthalein eliminated in the first twenty-four hour urine specimen in the form of conjugated phenolphthalein. The greater the cathartic action, the less the urinary elimination of phenolphthalein.

INFLUENCES DETERMINING THE ELIMINATION OF PHENOLPHTHALEIN

Attention was concentrated on the following factors as to their influence on the total amount of phenolphthalein (free and conjugated) eliminated: (1) cathartic action and size of the dose; (2) the method of its administration, and (3) the elimination on successive days after the dose.

1. *Relation of Conjugated Phenolphthalein Elimination to Cathartic Action.*—This relation is shown in chart 1, in which symbols indicate the percentage of phenolphthalein eliminated as compared with the amount ingested, when the results as to degree of evacuant action are considered. It is an interesting fact, as shown by this graph, that the presence or absence of cathartic action has a definite determining influence on the urinary elimination of phenolphthalein. There is a tendency—other things being equal—to an inverse relation between the two; i. e., the greater the cathartic action, the less the urinary elimination of phenolphthalein, and vice versa. This relation is also shown to be true for phenolphthalein in chart 2, which gives the results of the twenty-four hour elimination after 1,000 doses of phenolphthalein in our previous study [4] as well as by the "probability curve" of chart 3, based on this study. As shown in chart 3, the 50 per cent ordinate of the cases with cathartic action intersects the abscissas at 2 mg. and that of the cases with no cathartic action at 3 mg. It is obvious, when one scrutinizes chart 1, that the amount eliminated bears no proportion to the dose administered: that indeed, generally, the larger the dose the smaller a percentage of it is eliminated. This may seem paradoxical if it is not remembered that the greater the dose the greater the cathartic effect; hence the greater amount is lost in the stools and the lesser remains for elimination in the urine.

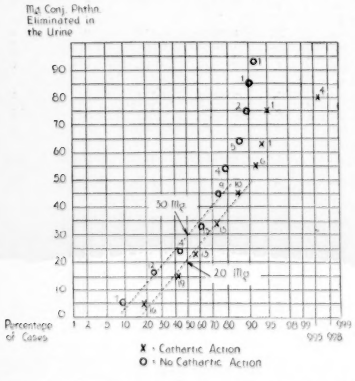

Chart 3.—Phenolphthalein conjugate elimination as influenced by cathartic effect, dose being constant (0.20 Gm.). Cathartic effect decreases the amount of conjugated phenolphthalein elimination. On "arithmetic probability paper" the milligrams of conjugated phenolphthalein in the first twenty four hours are placed in the abscissas, while the ordinates indicate the total percentage of cases, so that the 50 per cent line indicates the probability that there will be an approximately equal number of cases to either side of it. The actual number of determinations is indicated by the figures accompanying the respective points in the graph.

2. *Broken Dose Administration.*—The suggestion has been advanced to administer this rather insoluble cathartic in "broken dosage," similarly to the way in which calomel is so frequently given, with the hope of securing a more pronounced cathartic effect by better utilization of the solvent available. Such a result is by no means obtained in the case of phenolphthalein. The first four doses administered in this study amounted to 60 mg., each given at intervals of a week; the first dose (A) and the fourth dose (D) were each given in one capsule at bedtime, while the second dose (B) was given in two 30 mg. capsules, one taken at bedtime and one in the morning; the third dose (C) in four 15 mg. capsules, one taken at bedtime, one the first thing in the morning, and then one at intervals of four hours until the entire dose was consumed. We found that, in some instances, broken dosage resulted in diminution or absence of cathartic action, and in a greater urinary elimination of phenolphthalein (see "report of cases").

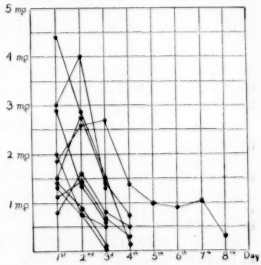

Chart 4.—Conjugated phenolphthalein elimination curves, after 60 mg. dose of phenolphthalein. The peak of elimination is reached in the second twenty-four hours and elimination ends with the fourth twenty-four hour specimen. It may continue longer when there is no cathartic action, as shown by the case in which the elimination lasted to the eighth day.

3. *The Phenolphthalein Elimination Curve.*—When the twenty-four hour phenolphthalein elimination in the urine is plotted after several doses, a curve is secured the composite of which for all the cases on the 60 mg. dose is shown in chart 4. It will be seen from this that, while the curves vary in detail, they agree among themselves in that with the majority of cases the peak of elimination is reached in the urine the second twenty-four hours and that in most instances it ends in the fourth twenty-four hour specimen. We find that this is true apparently irrespective of dose and the manner of its administration. There was an exceptional individual in whom the elimination continued up to the sixth or even the eighth day. In such a case no cathartic action was secured from any of these doses.

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193

CONCLUSIONS

1. In the urine, free phenolphthalein is generally absent or is present merely in traces after the usual medicinal doses, but it seems to be constantly present after large medicinal doses, i. e., doses above 240 mg., when the total elimination of free phenolphthalein may reach from 1 to 2 mg. in twenty-four hours.

2. Conjugated phenolphthalein is always present in the urine of persons taking phenolphthalein.

3. The total quantity of phenolphthalein eliminated (both free and conjugated) varies from 2.02 to 17.67 mg. after the giving of doses of from 60 to 480 mg.

4. The percentage of phenolphthalein eliminated of the quantity ingested varies from 1.41 to 19.7.

5. The larger the dose the smaller is the relative percentage of phenolphthalein eliminated, probably because the greater the cathartic action the less is the absorption.

6. The peak of elimination is reached on the first day in 44 per cent of the cases and on the second day in 52 per cent of the cases; a third day peak occurs in only 4 per cent of the cases and never beyond this time. In other words, it is reached practically in all cases within forty-eight hours after administration and it never exceeds seventy-eight hours. The duration of elimination does not, as a rule, exceed six days unless there is no cathartic action, when it may continue longer. Elimination usually ends by the fourth day, when there is cathartic action.

Clinical Notes, Suggestions and New Instruments

LYMPHOGRANULOMA AS A CAUSE OF PELVIC INFLAMMATORY DISEASE

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In a previous communication from these laboratories von Haam and D'Aunoy[1] reported that 33 per cent of females in a series suffering from venereal lymphogranuloma complained of pain in the lower lumbar and sacral regions, especially prominent when attempting to lie down. This symptom, which could be elicited in only 6 per cent of the males, they considered indicative of involvement of the deeper pelvic lymph glands, a common occurrence during the course of the infection in the female. In the same communication they suggested the possible etiologic significance of venereal lymphogranuloma in the production of chronic pelvic inflammatory disease, so frequently encountered in Negro women in this part of the country. Franchi[2] operated on a woman with venereal lymphogranuloma and acute pelvic symptoms; in the left tubo-ovarian region he found an inflammatory mass bound by numerous adhesions to the rectum and sigmoid and containing pus from which a potent Frei type antigen was prepared. We recently encountered a case of apparent simple salpingitis nodosa in which the microscopic changes were so suggestive of venereal lymphogranuloma as to warrant recording, even though, unfortunately, definite proof of the virus as the causal agent was not established.

REPORT OF CASE

History.—A Negress, aged 19, married, admitted to the Charity Hospital of Louisiana, complained of moderately severe pain in the lower part of the abdomen of six weeks' duration. The point of greatest intensity was in the right lower quadrant. The last menstrual period ended three weeks before admission. She had been pregnant on two occasions, the first pregnancy terminating in the delivery of a stillborn full term infant, the second in the birth of a full term child which lived only ten hours. She had had no abortions.

Examination.—Physical examination revealed that the patient was well developed and well nourished and apparently not acutely ill. The temperature was 99 F., pulse rate 72, blood pressure 130 systolic, 80 diastolic. Except for the pelvis, examination revealed no abnormalities. Marked tenderness was elicited in the right lower quadrant, and bimanual examination revealed a small mass in this region as well as tenderness of both adnexa. The cervix showed numerous erosions.

Laboratory examinations revealed hemoglobin 80 per cent (Sahli), sedimentation time twenty-five minutes, blood Wassermann reaction negative, urinalysis negative.

Course.—During her stay in the hospital her highest temperature was 99 F., and under conservative treatment she improved considerably, being discharged with the diagnosis of chronic cervicitis, chronic pelvic inflammatory disease and chronic appendicitis.

Fig. 1.—Section of a miliary abscess. Note the central area of necrosis, surrounded by a zone of epithelioid cells with a dense peripheral infiltration of plasma cells and lymphocytes.

Three months later she was readmitted because of persistence of pain in the right lower quadrant of the abdomen. Physical examination was essentially the same as on the previous admission. Both adnexa were still tender and a right adnexal mass was palpable. Sedimentation time was fifty-five minutes but otherwise the laboratory results were unchanged. A bilateral salpingo-oophorectomy and appendectomy were performed under spinal anesthesia. Except for pelvic adhesions the peritoneal cavity appeared normal. The postoperative course was uneventful.

Pathologic Examination.—The specimen consisted of two fallopian tubes, each of which measured 6 cm. in length, two ovaries and an appendix. Both tubes showed increased tortuosity, firm, thickened walls, fibrous adhesions on their serosae and patent, fimbriated ends, but the fimbriae were markedly thickened and blunt. The proximal portions were firm and nodular, measuring 1.5 cm. in diameter. A small amount of purulent material could be expressed from the surfaces exposed by sectioning through the nodular areas. The ovaries appeared normal and the appendix, except for a few serosal adhesions, was normal. The gross impression was chronic salpingitis nodosa.

From the Departments of Pathology and Bacteriology of the Medical Center of Louisiana State University and the Charity Hospital of Louisiana.

1. von Haam, Emmerich, and D'Aunoy, Rigney: Is Lymphogranuloma Inguinale a Systemic Disease? Am. J. Trop. Med. **16**: 527 (Sept.) 1936.

2. Franchi, F.: Su di un caso di parametrite causata dal virus della fo cadenite inguinal, Giorn. ital. di dermat. e. sif. **75**: 2003 (Dec.) 1934.

110
938

Sections taken through the nodular portions of the tubes showed many miliary rounded and stellate abscesses in the walls of the organs. The largest of these measured approximately 0.25 cm. in diameter. They were composed of central areas of liquefaction necrosis, containing polymorphonuclear leukocytes, scattered macrophages and necrotic unidentifiable cells and cellular débris. Surrounding these areas there were well formed zones of epithelioid cells in which an occasional irregular shaped, multinucleated giant cell was found. Beyond there were dense infiltrations of lymphocytes, macrophages, a few neutrophilic leukocytes and plasma cells, the latter predominating. In several instances a continuous tissue defect from an ulcerated area of the mucosa to a miliary abscess could be noted, the submucosa and musculature being replaced by a sparsely vascular, atypical granulation tissue infiltrated with plasma cells and macrophages. Inflammatory cells diffusely infiltrated the nonabscessed musculature, the subserosal tissue, the mesosalpinx and the serosal adhesions. Both perivascular and paravascular cellular infiltrations were observed, the latter frequently occurring as rather large, rounded collections of lymphocytes. Many of the arteries in the wall of the tubes and in the mesosalpinx showed marked adventitial and subendothelial connective tissue proliferation, some of them with slight and others with marked inflammatory cell infiltration of their walls. The lumens of many were markedly reduced in size and a few were completely occluded by this process. Both tubes were patent but the papillations were reduced in numbers, the papillae remaining being enormously thickened and blunt because of marked submucosal plasma cell infiltration. Except in the ulcerated areas, the mucosa was intact but consisted of flattened or cuboidal nonciliated cells. Superficial inclusions of epithelium resulting in pseudo-acinous formations were common. Sections stained by Gram's, Ziehl-Neelsen's, Giemsa's and Wright's methods failed to reveal micro-organisms.

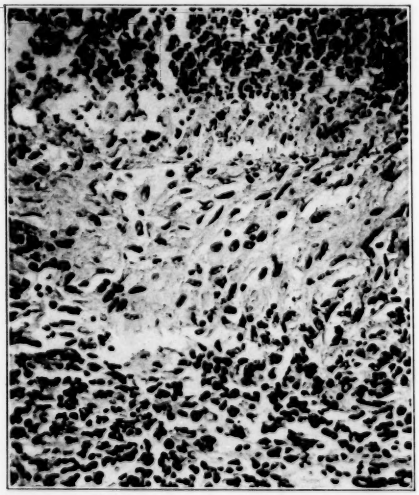

Fig. 2.—Section of the epithelioid cell zone with the pus cells and necrotic débris above and the peripheral lymphocytic infiltration below.

COMMENT

Since the histologic picture was so suggestive of the typical suppurative lesions of the lymph glands encountered in venereal lymphogranuloma, Frei tests were made on the patient with two different antigens, and both were strongly positive. The patient stated that she never had enlarged inguinal lymph glands. Careful examination failed to reveal inguinal buboes, rectal stricture or any significant lesion of the external genitalia.

SUMMARY

1. In a case of salpingitis with microscopic lesions consistent with those found in other organs during the course of venereal lymphogranuloma the patient was Frei positive and gave no other evidence of being or having been infected with the virus of venereal lymphogranuloma.

2. The case shows the necessity for considering venereal lymphogranuloma as an etiologic factor in pelvic inflammatory disease, particularly in the Negro race.

GONOCOCCIC MENINGITIS

RESULTS OF TREATMENT WITH SULFANILAMIDE

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Gonococcic meningitis is a very rare clinical condition, considering the fact that we have been able to find only twenty-two cases reported in the medical literature. Most of these reports were in foreign medical journals. Strictly speaking, one should not consider gonococcic meningitis as a separate and distinct primary disease entity, since it developed in the presence of an active gonococcic infection elsewhere in the body in each of the twenty-two reported cases. This is also true of the case to be reported in this article. Therefore this condition should be considered as a complication of a gonococcic infection occurring primarily in some other organ or system of the body. It may originate by metastasis from a gonorrheal vaginitis, urethritis, prostatitis, seminal vesiculitis, arthritis, ophthalmitis or any combination of these conditions, as well as of others.

It is believed that cases of gonococcic meningitis have been overlooked in the past, owing possibly to the mildness of the meningeal symptoms in occasional cases or to the fact that the meningitis was considered of meningococcic origin, the gonococcus and the meningococcus are so similar morphologically.

The first mention of nervous manifestations in cases of gonorrhea was made by Home [1] in 1805. Bradford and Kelley [2] and Strumia and Kohlhas [3] reported cases of gonococcic meningitis and reviewed the literature on this subject in 1933. Three of the cases reported in these reviews were in the new-born, two were in females and the remaining seventeen cases were in males between 19 and 60 years of age. There were ten deaths in the twenty-two cases, giving a mortality of approximately 45 per cent, showing that this disease or disease complication is a serious one as well as a very uncommon one. The rarity of this type of meningitis seems all the more remarkable, considering the prevalence of gonococcic infections. Blumer's [4] only mention of this condition is as follows: "It is generally assumed that involvement of the nervous system is toxic rather than metastatic, although such lesions as gonorrheal meningitis are undoubtedly due to metastasis."

We feel that the case we are presenting is of unusual interest in several respects, in addition to the fact that it presents a rare and serious complication of gonococcic infections. The patient was admitted to the hospital soon after the admission of two patients with meningococcic meningitis and was treated as such, including the administration of meningococcus antitoxin, during the first few days of hospitalization. This patient exhibited certain clinical and laboratory manifestations which were very much unlike those found in meningococcic meningitis and which led to additional bacteriologic studies. Moreover, the first Wassermann reaction of the spinal fluid was negative, whereas one taken two months later was positive. Sulfanilamide was used therapeutically after the organisms isolated from the spinal fluid were definitely identified as gonococci by means of careful morphologic, cultural, fermentation and agglutination studies, which are given in detail in a later paragraph.

From the Medical Service, Station Hospital, Fort Bragg, N. C.

1. Home, Everard: Practical Observations on the Treatment of Strictures in the Urethra and in the Esophagus, ed. 3, London, W. Bulmer & Co., 1805, vol. 2, pp. 11, 211, 271 and 276.

2. Bradford, W. L., and Kelly, H. W.: Gonococcic Meningitis in a New-Born Infant, Am. J. Dis. Child. **46**: 543-549 (Sept.) 1933.

3. Strumia, M. M., and Kohlhas, J. J.: Gonococcic Meningitis, J. Infect. Dis. **53**: 212-218 (Sept.-Oct.) 1933.

4. Blumer, George, in Cecil: Text Book of Medicine, ed. 3, Philadelphia and London, W. B. Saunders Company, 1935, p. 136.

REPORT OF CASE

History.—J. W., a Negro youth, aged 18, an enrollee in the Civilian Conservation Corps, was admitted to the genito-urinary service of the hospital May 21, 1937, because of a profuse purulent urethral discharge of ten days' duration. The family history and the past history were irrelevant. The patient reported that his last sexual exposure was May 1. He did not take any type of prophylaxis. A "kernel" developed in the left groin May 15, and he noticed some burning on urination. There had been no treatment of any kind prior to admission. There were no other symptoms.

Examination.—At the time of admission the patient was asthenic, well developed, fairly well nourished and in no acute distress. He was 67 inches (170 cm.) tall and weighed 115 pounds (52 Kg.). The skin was dry. The tonsils were enlarged and chronically infected. The left inguinal glands were moderately enlarged, discrete and tender. The heart, lungs and abdomen were normal. The blood pressure was 108 systolic, 68 diastolic. Neurologic examination was negative. There was marked phimosis and a profuse purulent urethral discharge. The prostate and seminal vesicles were normal. There were no other physical abnormalities.

The blood count revealed red blood cells 3,900,000, hemoglobin 70 per cent, white blood cells 6,400, neutrophils 72 per cent, lymphocytes 23 per cent, monocytes 4 per cent, basophils 1 per cent. The first glass of urine was cloudy, the second and third glasses were clear. Specific gravity was 1.018. Tests for albumin and sugar were negative. On microscopic examination there were many white blood cells and many intracellular and extracellular gram-negative diplococci. A smear from the urethra showed many white blood cells as well as many intracellular and extracellular gram-negative diplococci. The blood Wassermann reaction was two plus, the Kahn reaction four plus. The Wassermann test was repeated later with the same results.

The clinical diagnosis was (1) urethritis, acute anterior, gonorrheal; (2) phimosis; (3) tonsillitis, chronic, follicular, bilateral; (4) syphilis, tertiary; (5) anemia, secondary.

Progress in the Hospital.—May 23, the patient was to receive local treatment for urethritis, but he was not feeling well and treatment was delayed.

May 24 (three days after admission) the patient complained of severe generalized headache; he became nauseated, vomited and stated that he could not walk because his back, neck and legs were stiff. Examination at this time revealed no mental changes. The temperature was 103.5 F., the pulse 64, respiratory rate 16 and blood pressure 130 systolic, 80 diastolic. The white cells count was 6,500, with 71 per cent polymorphonuclear leukocytes. The neck was rigid and hyperextended. The Kernig sign was strongly positive bilaterally. The Babinski reflex was absent. A lumbar puncture was performed and 7 cc. of cloudy fluid spurted out. No more fluid could be obtained at this time. The pressure was not measured but was markedly increased. The cell count of the spinal fluid was 14,700. Globulin was four plus. A smear showed many intracellular and extracellular gram-negative diplococci. In spite of the many gram-negative intracellular diplococci, the patient was thought to have a meningococcic meningitis at that time and was transferred to the medical service, where therapy was instituted.

From May 24 to May 28 the patient received 110,000 units of meningococcus antitoxin intravenously as well as other symptomatic treatment, without any change in his condition. The temperature varied from 100 to 102.4 F. Blood counts remained about the same as the one made May 24. The pulse varied from 70 to 98, respirations from 18 to 22. Cell counts of the spinal fluid varied from 14,700 to 13,700, and the fluid continued to be cloudy. Stiffness of the neck remained unchanged, the Kernig reflexes were positive and the patient was perfectly rational and mentally normal in every way. He complained only of slight generalized headaches, which were partially relieved by daily spinal drainage of from 5 cc. to 12 cc. of fluid, since larger amounts could not be obtained. Cultures planted on 7.4 *p*H blood agar showed no growth after seven days' incubation at 37 C.

May 31, spinal puncture was performed with a spinal fluid cell count of 14,200. The complement fixation test for syphilis (Wassermann) on this spinal fluid was negative in all four dilutions. Globulin was normal and the colloidal gold curve was normal. Smears were positive for intracellular and extracellular gram-negative diplococci. Culture of the spinal fluid showed no growth on blood agar slants or in broth. Culture on a poured blood agar plate with ascitic fluid and incubated in a carbon dioxide jar at 37 C. for four days showed twelve small dew drop colonies which, on smear, revealed gram-negative diplococci. A colony was transferred to tubes of sugars and produced acid in dextrose but did not produce acid in maltose or other sugars. Agglutination tests with polyvalent antimeningococcus serum were negative. Agglutination tests with serum from a patient who had just recovered from gonorrheal urethritis, epididymitis and seminal vesiculitis were positive. Control tests were negative. Blood sugar was 86.9 mg. per hundred cubic centimeters. Nonprotein nitrogen was 26.7 mg. per hundred cubic centimeters. Fundus examination was negative.

Therapy with Sulfanilamide.—Realizing that gonococcic meningitis is a rare condition, that the mortality is high and that no specific treatment is known, we started the patient on small doses (0.324 Gm.) of sulfanilamide three times a day, commencing June 1. The temperature became normal and remained so all day for the first time June 12. It was normal on the 13th and 14th, so the sulfanilamide was discontinued at that time.

June 16 to June 30 the daily temperature fluctuations ranged from 98.6 to 102.6 F.

June 21, sulfanilamide 0.324 Gm. three times a day was again instituted, because of fever. The spinal fluid cell count was 8, having gradually dropped since May 28, at which time the count was 14,000.

June 26, stiffness of the neck was absent for the first time.

June 30 the temperature was normal. Sulfanilamide was discontinued. There was no stiffness of the neck.

June 30 to July 22 the temperature was normal. There were no symptoms or abnormal physical signs.

July 28, four Wassermann reactions of the spinal fluid were two plus, two plus, plus minus, negative. The cell count was 42. Globulin was two plus. The colloidal gold curve was 5555421100. Additional diagnosis: Syphilis, cerebrospinal (added).

July 22 to August 3 the temperature fluctuated from 98 to 101.8 F.

August 3 to August 12 the temperature fluctuated from 98 to 99.6 F.

August 12 to August 14, sulfanilamide 1.3 Gm. was given three times a day. The temperature was normal.

August 14 to August 18, sulfanilamide 0.65 Gm. was given three times a day. The temperature was normal.

The patient's temperature remained normal, the spinal fluid was free from organisms, and the patient exhibited no subjective symptoms or abnormal objective manifestations of any kind. He was considered cured of gonococcic urethritis and meningitis and started on antisyphilitic therapy. August 28 he was discharged from the hospital and will continue the antisyphilitic therapy at home.

COMMENT

This case of gonococcic meningitis has been very instructive, although we do not wish to draw too definite conclusions from one case. It has suggested several interesting features which, in addition to the facts brought out in the literature by the previously reported cases, are worthy of consideration. In contrast to most cases of meningococcic meningitis, the disease in this case ran a prolonged course of several weeks instead of several days. The pulse was moderately slow (from 64 to 98). The white blood counts remained within normal limits. Very little (from 7 cc. to 12 cc.) spinal fluid could be obtained at each drainage during the first month of illness, even though it was definitely under increased pressure on at least two occasions. The cell counts of the spinal fluid were very high, running from 14,700 to 13,700 during the first ten days. The patient never demonstrated any mental changes of any kind, was perfectly rational at all times and did not appear critically ill at any time. There was stiffness of the neck for over a month. During most of the illness his appetite was good, the bowels moved without catharsis or enemas, and he rested well. The Wassermann reaction of the spinal fluid was negative on the eighth day of the meningitis but positive on the sixty-sixth day. From this we conclude that the cerebrospinal syphilis became manifest during

110
938

the course of treatment for gonococcic meningitis and probably occurred after June 21, at which time the spinal fluid cell count was 8 and the test for globulin was negative.

SUMMARY

1. Gonococcic meningitis is a rare clinical condition; we have found only twenty-two previously reported cases.

2. In the case of gonococcic meningitis presented, recovery occurred.

3. Gonococcic meningitis occurs in the presence of, or secondary to, gonococcic infections in other parts of the body.

4. The mortality in the twenty-two reported cases was 45 per cent.

5. Several clinical and laboratory features are brought out which differ from those usually found in cases of meningococcic meningitis.

6. This patient was treated with 110,000 units of meningococcus antitoxin in addition to daily spinal drainage during the first five days of the disease without definite improvement.

7. Sulfanilamide was used therapeutically after the gonococcus was definitely proved to be the organism causing the meningitis. Although it seemed that the patient was improving during the periods of sulfanilamide administration, we feel that this was probably coincidental.

8. It is believed that other cases of this unusual complication of a very common infection have been overlooked in the past. Careful bacteriologic studies in cases of meningitis developing in the presence of a gonococcic infection may show this condition to be more common than now considered.

ANAPHYLACTIC REACTIONS FOLLOWING MEDICATION WITH PARENTERAL LIVER EXTRACT

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With the introduction of parenteral liver extract, a more effective treatment of pernicious anemia has resulted, with consequent benefit to many persons suffering from this disease. This has been especially true of those who were refractive to oral liver therapy, and the variety of symptoms complained of, as well as the constant low erythrocyte level in this group, has been overcome by injecting liver extract. However, because of the nature of the extract and at times even the preservative used, reactions have occurred. In 1931 Held and Goldbloom [1] reported a case of erythema nodosum following oral liver therapy. They were not convinced, however, that this was a true allergic reaction. Following the introduction of parenteral liver extract, Strandell and Hammar,[2] while studying patients refractive to oral liver medication, noted an urticarial eruption in one of their cases. In 1933 Murphy [3] reported its use in 1,000 cases, and he observed only two reactions. One of these patients exhibited nausea and urticaria following the twelfth injection. The Netherland investigators [4] have observed "disagreeable phenomena following injection of liver extract." They have used "Campolon" [5] or "Pernaemon" [6] and reactions to these have varied from slight, transient erythematous eruptions to severe asthmatic breathing with coincident tachycardia and hypotension. Engel [7] also observed similar states, but he was able to resume injections of liver extract after suitable desensitization. Grün [8] gave small but increasing doses of extract to one of his patients who exhibited such sensitivity and finally was able to use an adequate amount of material in treating his patient. In commenting on the possible sensitivity to liver extract, THE JOURNAL [9] mentions that reactions have occurred only twice in a large series of cases in one clinic. One of these patients suffered from asthma and an attack developed immediately following an intravenous injection of liver extract. One manufacturing concern [10] reports that only six or eight reactions following parenteral liver therapy have come to its knowledge during the several years it has manufactured such extracts.

That another factor in liver extract may cause undesirable manifestations is suggested by Milbradt.[11] He attempted to overcome sensitivity to "spirocid" in a child with congenital syphilis and found that a red, itching exanthem appeared after several injections of liver extract. On further study he discovered that the liver extract per se did not cause the eruption but that the preservative did. After testing several similar compounds he concluded that the benzene ring caused these untoward reactions, and this, of course, adds another substance for consideration in the unusual case.

Fortunately these reactions are rare and, because of this fact, it should not detract from the use of liver extract. Rather it should cause the physician to be on the lookout for evidence of sensitivity. Nevertheless, statements have been made that with liver extract the patient is "free from serum sickness and anaphylactic reactions." [12] The purpose of this report is to bring attention again to the fact that reactions may and do occur at varying times after parenteral treatment has been started and that, by due modification of the treatment, future untoward manifestations may be avoided.

REPORT OF CASE

C. H., a man, aged 39, a telephone cable splicer, first seen in March 1930, complained of weakness, a sore tongue and discomfort in the upper part of the abdomen. Aside from these complaints he had enjoyed excellent health since childhood. He had not received injections of horse serum in the past. The only significant fact in his family history was that his mother had died from pernicious anemia.

The patient was well built but pale. The essential abnormal conditions were smoothness of the edges of the tongue, with a raw, beefy appearance at the tip, and diminution of the vibratory sense of the extremities. There was no evident icteric tint to the sclerae nor was the liver or spleen palpable. Examination of the blood revealed: Hemoglobin (Sahli) 58 per cent, erythrocytes 2,820,000 cells per cubic millimeter, color index 1+, leukocytes 6,250 cells per cubic millimeter, polymorphonuclear neutrophils 63 per cent, polymorphonuclear eosinophils 1 per cent, polymorphonuclear basophils 1 per cent, lymphocytes 27 per cent, monocytes 8 per cent. The erythrocytes were well filled with hemoglobin, but with marked changes in size, macrocytes predominating. Moderate variations in shape were found, but no erythroblasts were observed. The leukocytes and platelets, aside from being reduced in number, revealed no striking changes from normal. There was complete absence of free hydrochloric acid on gastric analysis.

As a result of these observations the patient was ordered to take liver and liver extract by mouth, supplemented by dilute hydrochloric acid during meals. A prompt response resulted. The reticulocytes reached 38 per cent on the eighth day and after six weeks of medication the erythrocytes numbered 4,600,000 cells per cubic millimeter. There was a corresponding increase in his sense of well being, and the tongue and symptoms of weakness cleared up.

In January 1932 he complained of feeling tired, especially in the extremities and thighs, and his daily work was an effort. The erythrocyte count remained between four and five million cells per cubic millimeter even after ventriculin with

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2. Strandell, Birger, and Hammar, Emil: "Magenresistente" Fälle von Anaemia perniciosa, erfolgreich mit Campolon behandelt: Urtikaria als Komplikation, Acta med. Scandinav. **77**: 345, 1932.

3. Murphy, W. P.: Maintenance of Normal Blood in Pernicious Anemia by Means of Intramuscular Injections of a Solution of Liver Extract, Am. J. M. Sc. **186**: 271 (Aug.) 1933.

4. Geijskes, P. A. G.: Onangename verschijnselen na Toediening von Pernaemon, Nederl. tijdschr. v. geneesk. **80**: 1915 (May 2) 1936. Kuipers, F. C.: Overgevoeligheids reactie na Leverinspuiting, ibid. **79**: 2771 (June 8) 1935. Roovers, J. J. C. P. A.: Onangename Verschijnselen na Pernaemon inspuiting, ibid. **79**: 5148 (Nov. 2) 1935. Tausk, M.: Bijreacties na Inspuiting von Leverextracten, ibid. **80**: 749 (Feb. 22) 1936.

5. A parenteral solution of liver extract marketed by the Winthrop Chemical Company.

6. A solution of liver extract manufactured and marketed in Germany.

7. Engel, K.: Anafilaxia a. los Preparadas de Higado en un caso de anemia perniciosa, Bol. Asoc. méd. de Puerto Rico **25**: 326 (May) 1933.

8. Grün, Georg: Ueberempfindlichkeit gegen parenteral verabreichte Leberpräparate bei einem Fall von perniziöser Anämie, Wien. klin. Wchnschr. **47**: 751 (June 15) 1934.

9. Possible Sensitivity to Liver Extract, Queries and Minor Notes, J. A. M. A. **104**: 2019 (June 1) 1935.

10. Lederle Laboratories: Personal communication to the author.

11. Milbradt, W.: Ueber eine eigenartige scheinbare Allergie gegen Leberextrakt, Dermat. Wchnschr. **101**: 1595 (Dec. 21) 1935.

12. Wilson, J. A., and Carey, W. C.: Further Observations on Parenteral Liver Extract Therapy in Pneumonia, Am. J. M. Sc. **193**: 752 (June) 1937.

iron had been given in large doses. He was unable to regain the dexterity of his hands, so necessary in his work, and his legs would not respond to the usual demands of his occupation. Massage and other physical therapy resulted in only slight benefit.

His condition remained about the same until July 24, 1935, when parenteral liver extract was begun. His improvement began and the erythrocytes reached a normal level. November 23, after he had received the fifteenth injection of liver concentrate intramuscularly, he complained of feeling flushed, and his face and neck were more red than usual. This phenomenon lasted for about one hour. December 1 he again asked for a similar injection, because he had improved so much. A few hours later he experienced a generalized urticarial eruption and the following day the lymph nodes, particularly in the cervical and supraclavicular regions, but also in the axilla and groin, were enlarged and tender. Epinephrine was given to relieve the marked pruritus, and recovery was complete in one week.

Despite this experience, he returned December 10 and demanded a similar treatment. The nimbleness of his hands had returned and the weakness and instability of the extremities had gone away. He was warned of possible reactions but persisted in his demand. A fresh ampule of similar extract was then given in a dose of 1 cc. In a few minutes he broke out in a clammy, moist perspiration and typical asthmatic breathing with rhonchi throughout the chest followed. The pulse rate became accelerated and there was incontinence of the bladder. Epinephrine was immediately given and relief was obtained in a short time.

Following these manifestations he felt completely restored to normal. In view of the fact that he was refractory to oral liver medication, a new brand of liver extract was obtained and a small amount of diluted liver extract was given without reaction. The amounts were gradually increased until a few months later the full dosage was reached and no further reactions occurred.

In order to throw some light on what factor it might be that caused such reactions, scratch tests were made with beef, pork and horse meat, on the hypothesis that the liver used in the preparation of the parenteral extract was derived from these sources. Beef and pork caused no reaction, but a raised area 14 mm. in diameter with a zone of erythema around it resulted from the test with horse meat.

SUMMARY

In the case reported here complete relief was not obtained from oral liver extract and only when the parenteral extract was given intramuscularly did the erythrocyte count remain normal and the distressing symptoms disappear. Varying gradations of allergic response to some factor in liver extract resulted after fourteen injections without reaction. At first merely a slight erythema resulted, but as the injections were continued urticaria, enlargement and tenderness of lymph nodes occurred and finally an anaphylactic reaction occurred, characterized by asthmatic breathing, diffuse rhonchi in the chest and tachycardia. These symptoms were relieved by injections of epinephrine. Scratch tests indicated possible sensitivity to horse meat, and it is probable that the first extract used was derived, at least in part, from horse liver. When the treatment was modified by the use of small but increasing amounts of extract, no reactions resulted. It is possible, however, that the allergic factor may not have been present in the new extract used.

CONCLUSIONS

1. Complete relief from symptoms and restoration to normal erythrocyte levels may not always result from the use of oral liver medication but can be obtained when the parenteral extract is used.

2. Reactions do occur in susceptible individuals. They may appear after the first injection but are often delayed until a number of such treatments have been given.

3. Such manifestations are apparently of an allergic nature.

4. Due care must be observed when mild reactions occur, and a proper modification of treatment should then be used.

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NODULAR GOITER OF THE NEW-BORN WITH SUBSEQUENT ADENOCARCINOMA

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From an etiologic aspect as well as from the standpoint of rarity, the occurrence of goiter in infants is of interest. It is known that the thyroid glands of infant cretins are often from two to five times normal size in endemic regions.[1] The pathologic change in these glands is essentially a diffuse vascular or parenchymatous enlargement, according to Kaufmann,[1] Boothby and Plummer [2] and others. Aschoff [3] and De Quervain [4] mentioned diffuse hyperplasia of the thyroid in the new-born ("struma, diffusea neonatorum") and Helmholz [5] has seen frank exophthalmic goiter in a child of 1 year.

Section of the adenocarcinoma in the nodule.

We are not aware, however, of any reports in the literature of a single large encapsulated adenoma occurring in a new-born child. Pemberton [6] has seen a diffuse adenomatous colloid goiter which was said to be present at birth. C. H. Mayo [6] recently told one of us (Stevens) that he had not seen a congenital nodular goiter in the human being but that, when a young man, he had discovered the condition in a litter of four puppies. He operated on one of the animals and confirmed the diagnosis of goiter. Kaufmann makes the statement that true adenomatous goiter does not appear in children, and Aschoff said that he had never seen the condition until after changing of the teeth. We report such a case. The interest in this case is increased by the discovery of an adenocarcinomatous area within the adenoma seven years after birth.

1. Kaufmann, Edward: Pathology, Philadelphia, P. Blakiston's Son & Co., 1929, vol. 1. Isenschmidt, Kloeppel, Sanderson-Dambier, quoted by Kaufmann.
2. Boothby, W. M., and Plummer, H. S.: Diseases of the Parathyroid and Thyroid Gland, Rochester, Minn., Schmidt.
3. Aschoff, Ludwig: Lectures on Pathology, New York, Paul B. Hoeber, Inc., 1924, pp. 319-331.
4. De Quervain, Fritz: Goitre, New York, William Wood & Co., 1924.
5. Helmholz, H. F.: Goitre in Children, Philadelphia, W. B. Saunders Company **18**: 537, 1936.
6. Personal communication to the authors.

REPORT OF CASE

A girl, aged 7 years, was brought to us because of a lump in her neck which had been present since birth. The parents stated that the tumor had not changed in size. This was subsequently confirmed by Dr. Samuel King of Fort Stanton, N. M., who delivered the child. Her voice had been a little husky as long as the parents could remember. Other than this and the presence of the tumor, the child had always seemed perfectly normal, both mentally and physically. The family had always lived in New Mexico and none had goiter. Examination revealed a firm smooth rounded mass about the size of the child's fist apparently attached to the left lobe of the thyroid. The mass moved with deglutition. No bruits or thrills were detected. There was no evidence of hyperthyroidism. Some dysphonia was present but the vocal cords were normal. Routine laboratory tests were negative and the child appeared to be in general good health.

Operation was performed by one of us (Stevens), assisted by Dr. Samuel King and Bennie Jensen. A large spherical encapsulated mass was found to originate from the left lobe of the thyroid at the inferior pole. The recurrent laryngeal nerve was adherent to the capsule of the mass at a point near the entrance of the inferior thyroid artery to the gland. The nerve was gently freed from the capsule, which relieved its apparent tension. The inferior thyroid vessels were ligated and the mass was subsequently removed without difficulty.

PATHOLOGY

The pathologic examination was performed by Dr. Willis Waite.

The specimen consisted of an encapsulated globular mass measuring 70 by 60 by 50 mm. and weighing 88 Gm. On section the tissue structure was fairly homogeneous and semitranslucent except for one pale grayish pink area well within the capsule.

Histologic section showed a growth of adenomatous tissue bordering on normal thyroid tissue, with the exception of the section through the pale area. This section was examined also by Drs. Broders, Kernahan and Robertson of the Mayo Clinic, all of whom concurred in the diagnosis of grade 2 adenocarcinoma. Although glandular arrangement was for the most part in evidence, the presence of mitosis, irregular cell nuclei with prominent and relatively large nucleoli and invasion of the venules by the cells established the diagnosis of malignancy.

The patient made an uneventful convalescence and was dismissed from the hospital on the fourth postoperative day. The postoperative check showed the vocal cords to be normal. At the present time, two years after the operation, the child's voice is normal and the child is well.

COMMENT

This case, although of interest chiefly because of its rarity, probably merits comment because of the etiologic factors involved. The child's parents did not have goiter. The mother was in good health at the time of the birth of the child. The child was born and raised and her parents have always lived in New Mexico, which is notably not in an endemic goiter region. The theories of lack of iodine and of infection, then, do not seem plausible in this case. Woelfler,[7] who contributed much to the subject of adenomas of the thyroid, believed that they develop from fetal rests. It is, however, questionable whether any one has actually traced such a development. The presence of a single large adenoma projecting from the thyroid gland of this patient at birth and the absence of known predisposing factors seem to support Woelfler's theory, at least to the extent that certain adenomas may develop from embryonal tissue. This case seems to throw additional light on the question of whether or not cancer develops from primarily benign adenomatous tissue. Certainly it seems logical to assume that this was originally a benign adenoma of the thyroid, since an adenocarcinoma could hardly be considered to be nonprogressive for seven years, as was this nodule. Therefore one would conclude that the adenocarcinoma in this case had recently developed from simple adenomatous tissue.

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7. Woelfler, quoted by Boothby and Plummer.[3]

THE USE OF THE LOW SALT DIET IN THE DIAGNOSIS OF ADDISON'S DISEASE

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The use of a salt free diet for four or five days to aid in the diagnosis of Addison's disease in doubtful cases has recently been advocated. The precipitation by such a diet of a typical clinical crisis with accompanying changes in the chemistry of the blood is considered confirmatory. An adequate supply of potent cortical extract as well as intravenous salt solution must be kept on hand in the event of a severe crisis which appears to threaten life.

The following case is reported to show that the salt free diet may be a dangerous expedient, since sudden death may occur without the development of critical symptoms.

REPORT OF CASE

History.—H. L., a man, aged 52, Austrian, complained of dyspnea and weakness for three and a half months. He had a chronic nonproductive cough, had lost 15 pounds (6.8 Kg.) during this period and had noted constipation for three weeks. On the day of admission the patient became dizzy, had black spots before the eyes, and vomited.

The past history was essentially irrelevant except for an illness diagnosed as pneumonia in 1923, during which tapping of the chest on the right side yielded clear fluid.

The family history was noncontributory; the father died of unknown causes; the mother was 80 years old and in good health. Three brothers and sisters were living and well. There was no familial tuberculosis, cancer, diabetes, kidney or heart disease, nor was there any evidence of allergy.

Examination.—The patient was well developed and well nourished and had a dusky and somewhat violaceous tinge to his skin. There was no orthopnea or apparent dyspnea. There was slight and somewhat questionable pigmentation of the mucous membrane of the right cheek and on the dorsum of the tongue. The pupils were equal and regular and reacted to light and in accommodation. The extra-ocular movements and the sclerae were normal. The fundi showed no changes. The ears, nose and throat were normal. A few remaining teeth were carious. The trachea was in the midline. There was no adenopathy or thyroid enlargement. The heart was normal in size, the sounds were clear, and there were no murmurs. The pulmonic second sound was equal to the aortic second sound. There was regular sinus rhythm. The blood pressure was 100 systolic, 70 diastolic. The peripheral vessels were in good condition. There was slight impairment of resonance and diminution of breath sounds over the right upper part of the chest posteriorly. A few râles were heard over the right upper part of the chest anteriorly. Examination of the abdomen showed no masses, tenderness or increased resistance. The rectal examination was negative. The prostate was normal. There was moderate clubbing of the fingers and definite cyanosis of the finger tips. The neurologic examination was negative except for bilateral ankle clonus and a questionable bilateral Babinski reflex.

Laboratory studies revealed the following: The urine was clear, acid, with a specific gravity of 1.020, albumin 0, sugar 0, and no microscopic changes. Blood count: Red blood cells 4,900,000, hemoglobin 103 per cent, white blood cells 7,700, polymorphonuclear leukocytes 70 per cent, lymphocytes 25 per cent, monocytes 5 per cent. Two days later the hemoglobin was 110 per cent. The Wassermann reaction was negative.

Blood chlorides were 356 mg. per hundred cubic centimeters.

A sugar tolerance test could not be completed because the patient vomited the dextrose. The fasting blood sugar was 83 mg. per hundred cubic centimeters. examination of the blood showed 10 per cent methemoglobin.

Gastric analysis: Fasting specimen showed no free hydrochloric acid; total acidity 4. Fifty-five minutes after administration of histamine, free hydrochloric acid was present and the total acidity increased to 70.

X-ray examination of the chest revealed a productive infiltration, tuberculous in type, involving the apical and subapical regions of both lungs.

From the Second (Cornell) Medical Division of Bellevue Hospital and the Department of Medicine, Cornell University Medical College.

A flat x-ray plate of the abdomen did not show calcification of the adrenals and was negative in other respects.

An electrocardiogram showed diphasic T waves in leads 1 and 2.

The basal metabolic rate was minus 2.3 per cent.

The spinal fluid contained 6 lymphocytes per cubic millimeter and was negative for albumin. The Wassermann and colloidal gold tests were negative.

Course.—The temperature and pulse were normal except on one occasion when there was a rise in temperature to 102.4 F. accompanied by headache and numbness of the legs. The blood pressure ranged between 100 systolic, 70 diastolic and 90 systolic, 60 diastolic. The patient's appetite was poor and he complained in general of not feeling well. If he attempted to stand or even to sit up, a complete vasomotor collapse was induced; the pulse would become rapid and weak, the blood pressure would drop abruptly so that a reading could not be obtained and the patient became very pale and perspired profusely.

In view of the fact that the diagnosis of Addison's disease might be contested on the ground that the pulmonary tuberculosis per se could account for the entire picture, and since the general discoloration of the skin could have been explained by the methemoglobinemia, the patient was put on a salt free diet in order to precipitate a crisis and to aid in the establishment of the diagnosis of Addison's disease. There was no perceptible change in the patient's condition after four days on this regimen and it was decided to discontinue the salt free diet and to administer salt intravenously and by mouth the next day We were, however, not given this opportunity At 3:40 a. m. the following day the patient complained of pain in the left side of the chest anteriorly which did not radiate. The heart sounds were somewhat weak but the patient did not seem very ill The pain was apparently relieved by the administration of 10 grains (0.65 Gm.) of acetylsalicylic acid and one-half grain (0.03 Gm.) of phenobarbital. The patient slept from 3:50 until 4 a. m. At this time he awakened and seemed restless but made no complaints. He was left for a few moments by the nurse and on her return was found dead.

Autopsy.—This was performed by Dr. Milton Helpern of the Medical Examiner's Office, through whose courtesy the following summary of the pertinent observations is added:

The heart was normal in size and weighed 330 Gm.; the valves were flexible and natural in appearance. The coronary arteries showed a moderate degree of sclerosis with no stenosis or occlusion. The endocardium was smooth. The aorta showed a slight amount of sclerosis and loss of elasticity. The lungs presented numerous adhesions. The upper left lobe showed much scarring of the parenchyma with depression of the visceropleura. On section there was overgrowth of interstitial connective tissue and an area of tuberculous infiltration marked by grayish brown pigmentation. There was similar involvement of the upper portion of the left lower lobe with clusters of conglomerate tubercles. The right lung showed extensive fibrous distortion of the parenchyma and bronchi in the upper lobe with nodular induration and contraction of the tissues. There was also some interstitial fibrosis in the middle lobe. There was no fresh caseous tuberculosis in either lung, the process being essentially a fibrotic one in the right lower lobe and a productive one in the left.

Examination of the gastro-intestinal tract showed that the esophagus was normal. The stomach showed merely some postmortem digestion. The intestine and appendix were normal. The liver and spleen were slightly enlarged and congested. The pancreas was normal. The adrenals were indurated. On section there appeared to be almost complete replacement by fibrocaseous tuberculosis. The right adrenal was 2¼ inches (5.7 cm.) long, 1 inch (2.5 cm.) wide and nine-sixteenths inch (1.4 cm.) thick and was firmly adherent to the surrounding fat tissue. No cortical substance could be made out. The left adrenal was slightly smaller and showed similar changes. The kidneys were slightly increased in size and showed congestion with exaggeration of the markings. The pelves, ureters and bladder were normal. The prostate and testes were normal in size and showed no tuberculous involvement.

Examination of the skull showed no injury. The dura was intact and slightly adherent at the base. There was some pial edema and congestion. The vessels at the base of the brain showed slight sclerosis. The pons, cerebellum, brain stem and basal ganglions were intact. The pituitary was normal.

Microscopic Examination: The myocardium was normal; there was intimal thickening of the coronary arteries; the aorta showed no changes. The lungs showed multiple areas of fibrosis with small areas of caseation in some of them. There were many giant cells and tubercles, some conglomerate. There were focal collections of lymphocytes, especially at the periphery of the fibrosis, and some small areas of hemorrhage. The surrounding alveoli showed considerable congestion with diapedesis of red cells into the alveolar spaces, accompanied by large mononuclear phagocytes. The arteries in the area of fibrosis showed a moderate amount of intimal proliferation.

Sections of the spleen showed only congestion. The liver showed congestion and moderate fatty degeneration. The pancreas showed autolysis and slight interlobular fibrosis. Some sections of the adrenal showed complete replacement by a caseous mass undergoing some calcification and enclosed in a thick avascular fibrous capsule having focal and general round cell infiltration with no tubercles or giant cells. Other sections showed marked engorgement and autolysis of the cells but appeared to contain all the layers.

The kidneys showed normal architecture with some engorgement of the glomerular capillary tufts. A few of the small arteries showed slight intimal thickening.

The bone marrow was normal on section.

COMMENT

It is well known of course that sudden death is common in Addison's disease, and its occurrence in this case may have been entirely fortuitous. Nevertheless, we regretted that we had not applied the therapeutic test rather than the purely diagnostic one.

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110
938

Special Articles

THE PHYSIOLOGY OF VITAMIN B_1

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This article and others recently published or to be published comprise a new series on the present status of our knowledge of the vitamins. They have been prepared under the general auspices of the Council on Pharmacy and Chemistry and the Council on Foods. The opinions expressed are those of the authors and not necessarily the opinions of either council. The articles will be published later in book form.—ED.

As the papers of this series are planned to be a continuation of those of an earlier series, no attempt will be made here to review at all completely the voluminous literature bearing on the physiology of vitamin B_1. The historical development of the subject, the various methods which may be followed in assaying for this vitamin, the importance of the vitamin for growth, lactation and other functions, and similar topics concerning which our fundamental knowledge has been established for many years—all of these will be omitted from the present discussion. Instead, the objective will be to survey briefly the more recent contributions to knowledge in this field, to summarize as briefly as possible the present points of view concerning the relation of vitamin B_1 to various bodily functions, to describe the unique function of this dietary factor, if there is such, and, finally, to indicate wherever possible the significance in medicine and practical dietetics of our present knowledge.

DISTRIBUTION OF VITAMIN B_1 IN THE BODY

It is conceivable that knowledge of the relative distribution of vitamin B_1 in the body may assist in our understanding of its possible functions. We are concerned here not with the usefulness of such information in relation to relative food values of the various tissues but rather with its bearing on the function of vitamin B_1.

The earlier literature on this subject emphasized a similarity of distribution of the so-called nucleins and vitamin B_1, and on this observation was based the idea that this dietary essential has some important role in the functioning of every cell rather than in the activity of a special organ or tissue system. More recent studies have enlarged the body of available data without seriously altering the conclusions drawn from them. Westenbrink [1] performed feeding experiments with the tissues of normal and B_1 deficient rats and found the heart, liver and kidney to have the highest content of vitamin B_1 under normal conditions, the last two organs evidently acting as storehouses for the dietary factor. All of the organs examined except the brain were observed to suffer great diminution in their vitamin B_1 content after the rats had subsisted for five weeks on the B_1 free diet. Essentially similar results were obtained by Graham and Griffith.[2] In this connection it is pertinent to say that in 1923 Nagayo [3] cited the presence of vitamin B_1 in the tissues of patients who had died of beriberi as strong evidence for the view that beriberi is not due essentially to vitamin B_1 deficiency. I do not believe that the validity of the deficiency disease theory requires that the tissues become absolutely devoid of the vitamin before characteristic symptoms and pathologic changes may occur, but merely that the concentration in the various organs, or perhaps in certain special organs, must become less than a critical or threshold value. Furthermore, it is reasonable to believe that the different organs will respond to the condition of low vitamin supply in various ways. Such a point of view appears consonant with all the data now at hand.

The amounts of vitamin found in the various tissues under different dietary regimens support the conclusion that the organism's capacity to store vitamin B_1 is limited. In the pigeon, the rat and the dog, the time required for a shortage of vitamin B_1 to become evident varies from about ten days to three or four weeks, the latter period being characteristic of the largest of these species, the dog. This limited capacity for storage is obviously of great importance in relation to clinical situations as well as in practical dietetics and hygiene.

Students interested in the quantitative aspects of this topic will find the data of Brodie and MacLeod [4] worthy of examination. These investigators reported that in animals subsisting on normal diets the liver is found to contain about ten times as much vitamin B_1 per gram as voluntary muscle; the kidney is about one-half and the brain approximately one-third as rich per gram as voluntary muscle. The heart is almost as rich as the liver. Only traces of the vitamin are found in the blood, spleen and lungs. It was found that within certain limits the vitamin B_1 content of the body is undoubtedly influenced by the amount of vitamin in the diet, a conclusion harmonizing well with the results of many other types of investigations.

The suggestions in the literature (1) that vitamin B_1 functions in some way in the metabolism of one or more of the energy-yielding foodstuffs, probably carbohydrate, and (2) that fat in some way "spares" vitamin B_1 (discussed later in this paper) led Westenbrink [5] to study the disappearance of vitamin B_1 from certain organs of pigeons subsisting on B_1-free, carbohydrate-rich, fat-poor diets as compared with those subsisting on B_1-free, carbohydrate-free, fat-rich combinations of food. In view of his results, Westenbrink considered it unlikely that the appearance of polyneuritis after shorter or longer periods of the feeding of large amounts of carbohydrate or fat can be explained as due simply to the more rapid or slower disappearance, respectively, of vitamin B_1 from the organism. Some other factor seems to be involved.

For some time it has been known that vitamin B_1 is present in the urine and that the amount may vary with that furnished in the diet, a plethora of vitamin in the blood and the entire body evidently being associated with increased elimination of the dietary essential through the kidney. As the vitamin is water soluble, its presence in the urine is easily understood. The fact that the amount thus eliminated can vary with that available within the organism is important to the physiologist and the clinician. On it one may base a search for a vitamin B_1 function test by which to detect persons who do not have their tissue reservoirs "saturated" with the vitamin. This fact is also important because on it rests the possibility that vigorous activity of the kidney, as for example in pronounced diuresis, may mean an increased elimination of vitamin B_1 from the body, to its possible detriment. Tests of this possibility by experiments with dogs [6] have in fact yielded positive results.

Harris and Leong [7] and others have examined experimentally the possibility of a vitamin B_1 function test based on quantitative examination of the urine secreted under definite conditions. The reader is referred to the original papers for details. Let it suffice to state here that, in the opinion of these investigators, "a daily excretion of less than 12 international units (corresponding with an average concentration of 1 I. U. per 100 cc. raises the presumption that the diet contains less than a normal allowance of vitamin B_1." With the isolation and synthesis of pure vitamin B_1, and therefore its availability, and the perfection of microchemical methods by which to analyze the urine for this factor, it is likely that other vitamin B_1 function tests will be devised which are accurate yet more saving of time in their performance. The application

1. Westenbrink, H. G. K.: Ueber den Gehalt an Vitamin-B_1 der Organe von weissen Ratten bei normaler und Vitamin-B_1-freier Ernährung, Arch. néerl. de physiol. **17**: 560-577, 1932.

2. Graham, Claire, and Griffith, W. H.: Vitamin B_1 and B_2 in Tissues of Normal and Experimental Rats, Proc. Soc. Exper. Biol. & Med. **29**: 695-697 (Feb.) 1932.

3. Nagayo, Mataro: Beriberi and Rice Neuritis, J. A. M. A. **81**: 1435-1437 (Oct. 27) 1923.

4. Brodie, Jessie B., and MacLeod, Florence L.: Quantitative Experiments on the Occurrence of Vitamin B in Organs, J. Nutrition **10**: 179-186 (Aug.) 1935.

5. Westenbrink, H. G. K.: Ueber das Verschwinden des Vitamins-B_1 aus einigen Organen von Tauben bei Vitamin-B_1-freier, kohlehydratreicher, fettarmer Nahrung, bezw. bei Vitamin-B_1-freier, kohlehydratfreier, fettreicher Nahrung, nebst einer Vergleichung des Vitamin-B_1-Gehaltes von Organen von Ratten und Tauben, Arch. néerl. de physiol. **19**: 116-121, 1934.

6. Cowgill, G. R.; Rosenberg, H. A., and Rogoff, J.: Studies in the Physiology of Vitamins: XIV. The Effect of Administration of Large Amounts of Water on the Time Required for the Development of the Anorexia Characteristics of a Deficiency of the Vitamin B Complex, Am. J. Physiol. **95**: 537-541 (Dec.) 1930.

7. Harris, L. J., and Leong, P. C.: Vitamins in Human Nutrition: The Excretion of Vitamin B_1 in Human Urine and Its Dependence on the Dietary Intake, Lancet **1**: 886 (April 18) 1936. Helmer, O. M.: Vitamin B_1 and B_2 Content of Human Urine, Proc. Soc. Exper. Biol. & Med. **32**: 1187 (April) 1935. Roscoe, Margaret H.: The B Vitamins in Human Urine, Biochem. J. **30**: 1053 (June) 1936.

of such methods in the survey of patients in the clinic and in representative groups of the normal population should result in numerous interesting and valuable observations.

VITAMIN B_1 AND THE ALIMENTARY TRACT

Recent additions to the literature bearing on vitamin B_1 and the alimentary tract have not been such as to warrant any serious changes in the view held hitherto, that lack of vitamin B_1 does not produce any specific dysfunction of the organs of the alimentary tract. Sure and Thatcher [8] were able to confirm an earlier report [9] that gastric ulcers appear in a large percentage of white rats subsisting on a B_1-deficient diet and therefore suggested that vitamin B_1 therapy may be indicated in the treatment of gastric ulcers in human beings. The failure to secure ulcers in practically every case, however, constitutes an argument in favor of the view that the ulcers arise secondarily in the course of vitamin B_1 deficiency, probably as part of the response of the stomach to a generalized systemic condition and not because the function of vitamin B_1 is specific in relation to this organ.

Babkin [10] has reported interesting observations suggesting a relation of vitamin B_1 or some other member of the B complex to the nervous mechanism controlling gastric secretion. Dogs and cats, suitably operated on so as to permit experiments of the sham feeding type, were allowed to subsist on a diet deficient in the B complex and then were tested for their gastric responses to sham feeding, subcutaneous injections of histamine and the presence of food and 5 per cent alcohol solution in the intestine. During the state of vitamin deficiency there was a marked diminution in the response of the gastric glands to all of these stimuli. When yeast was administered the responses became normal within a few days. The effective agent in the yeast was not determined. These results are of interest because they suggest a possible explanation of the anorexia so characteristic of vitamin B deficiency. It will be recalled that earlier attempts to explain this anorexia by study of the effects of vitamin B deficiency on the so-called hunger contractions of the empty stomach,[11] while yielding interesting results, nevertheless failed to furnish the desired explanation. The origin of this anorexia still remains an unsolved problem.

Studies have been made of the efficiency with which various enzymes of the alimentary tract can function in the presence of vitamin B deficiency. Sure and his associates [12] reported in vitro experiments indicating that no impairment of tryptic and ereptic digestion of casein is associated with B deficiency. Such a result conforms well with those recorded in the earlier literature. With respect to the activity of pancreatic lipase, however, a pronounced decrease was noted. The significance of these in vitro results is questionable in view of the in vivo observations of Salmon and Goodman [13] that in rats there is no impairment in the digestion of fat as a result of vitamin B_1 deficiency.

Reder and Gallup [14] reported that rats lacking both vitamin B_1 and vitamin G exhibit slower digestion and absorption of administered carbohydrate than normal control animals. When vitamin B_1 is added to the diet the rate does not improve; however, the addition of vitamin G to the ration proves effective. These results, apart from their significance in relation to the theme under discussion, emphasize to the investigator in this field the importance of planning his experiments so as to be able to attribute his results more specifically to vitamin B_1 or other well defined members of the B complex.

As anorexia is a common characteristic of vitamin B_1 deficiency and its presence necessarily means some degree of inanition, students of the physiology of vitamin B_1 have learned to appreciate the importance in their experiments of making simultaneous observations on control animals receiving the vitamin but restricted in their intake of the basal diet to the amount ingested voluntarily by the B_1-deficient animals. When such control observations are made, it is astonishing how many of the differences from normal function that have been reported have proved to be nonspecific, appearing in the undernourished control animals as well. This proved again to be the case in the recent work reported by Chatterjee,[15] who studied the motor functions of the intestine in the presence of B_1 deficiency. In both the vitamin-deprived and the starved animals there was a definite decrease in the amplitude, the number and the intensity of the intestinal contractions, as well as in the responses to pilocarpine, atropine, nicotine and barium chloride.

Molitor and Sampson [16] have tested the influence of pure vitamin B_1 on intestinal motility, using isolated rabbit's intestine suspended in Ringer's solution as well as taking observations of the intestine in situ. The experiments included study of the contractions under normal conditions and after the movements had been paralyzed with papaverine. The addition of pure vitamin to the Ringer solution, as well as the intravenous injection of vitamin in the in situ experiments, was without any effect on the movements. Evidently, then, this agent, unlike various drugs, has no demonstrable effect on the intestine of the normal organism; its action is exerted up to the point required by the animal but not beyond.

Vitamin B_1 is readily absorbed from both the small and the large intestine, and in all probability people may vary with respect to the efficiency of such absorption. When making vitamin B_1 assays with pigeons by a technic involving the administration of materials by way of the crop, I [17] have frequently found a bird which requires much more vitamin B_1 than other comparable birds of a series. This difference may theoretically be due to less efficient absorption, but it might also be the result of a more ready elimination through

8. Sure, Barnett, and Thatcher, H. S.: Avitaminosis: XIV. Production of Gastric Ulcers in the Albino Rat as a Result of Specific Influence of Deficiency of Vitamin B, Arch. Path. **16:** 809-816 (Dec.) 1933.

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10. Babkin, B. P.: Nervous Control of Gastric Secretion and Effect of Vitamin Deficiency on Its Production, Canad. M. A. J. **29:** 5-9 (July) 1933.

11. Cowgill, G. R.; Deuel, H. J., Jr.; Plummer, N., and Messer, F. C.: Studies in the Physiology of Vitamins: IV. Vitamin B in Relation to Gastric Motility, Am. J. Physiol. **77:** 389-401 (July) 1926.

12. Sure, Barnett; Kik, M. C., and Buchanan, Kathryn S.: Enzymic Efficiency in Avitaminosis: I. Influence of Vitamin B Deficiency on Tryptic and Ereptic Digestion of Casein, J. Biol. Chem. **108:** 19-26 (Jan.) 1935; II. Influence of Vitamin B Deficiency on Efficiency of Pancreatic Lipase and Esterase, J. Biol. Chem. **108:** 27-33 (Jan.) 1935.

13. Salmon, W. D., and Goodman, J. G.: Alleviation of Vitamin B Deficiency in the Rat by Certain Natural Fats and Synthetic Esters, J. Nutrition **13:** 477-500 (May) 1937.

14. Reder, Ruth, and Gallup, W. D.: The Rate of Digestion and Absorption During Avitaminosis B and G, Proc. Oklahoma Acad. Sc. **15:** 58-61, 1935.

15. Chatterjee, D. D.: Motor Functions of the Bowel in Avitaminosis B and in Starved Animals, Indian J. M. Research **23:** 191-198 (July) 1935.

16. Molitor, H., and Sampson, W. L.: Personal communication to the author from the Merck Laboratory of Therapeutic Research, Rahway, N. J.

17. As an illustration see pigeon 25, table 2, page 37, in Cowgill, G. R.: The Vitamin B Requirement of Man, New Haven, Conn., Yale University Press, 1935.

110
938

the kidney or more rapid consumption in metabolic processes. Some observations [18] have been made of the absorption of various vitamin B_1 products when placed in the large intestine of the dog through a valvular cecostomy. From such experiments it appears that vitamin B_1 is not readily eluted from a fullers' earth adsorbate in the large intestine, and such a product therefore is less effective than others which contain the vitamin already dissolved in a suitable aqueous medium. These observations are of significance to clinicians who may desire to give vitamin B_1 to patients having a fistula in the large intestine. Evidently not all vitamin B_1 products are of equal value for such therapeutic use.

Even when administered by mouth, products of the type of fullers' earth adsorbate, such as the present international vitamin B_1 standard, do not give up all of their adsorbed vitamin when passing through the alimentary tract. Sampson and Keresztesy [19] have been able to show that elution with quinine sulfate solution yields approximately twice as much vitamin as elution by the older methods involving alkaline solutions. In the light of these facts it is reasonable to assume that the variable biologic effects reported by workers using adsorbates are due to different degrees of elution of the vitamin within the intestine.

It is theoretically possible that vitamin B_1 may be lost from the body under the conditions of chronic diarrhea. This question has been examined experimentally.[20] It appears that diarrhea merely causes some failure of absorption of an appreciable fraction of the ingested vitamin; it does not cause an excretion of vitamin B_1 from the organism through the intestinal wall into the lumen of the intestine.

The presence of vitamin B_1 in the feces has led many investigators to endeavor to determine its origin. In view of the observations of numerous workers it appears likely that this vitamin is synthesized by certain bacteria and other micro-organisms. Bechdel and his associates [21] reported that the cow is able to synthesize vitamin B_1 in its rumen through the activity of certain bacteria and thus derive the benefits of the synthesized products without the necessity of reingestion of feces, as is the case with the rat and other animals. In the case of the rat it appears from the work of Guerrant and his collaborators [22] that the type of carbohydrate in the ration has some role in this process. Sucrose, dextrose and starch, being usually assimilated quite rapidly, rarely reach the cecum in appreciable amounts, and it was shown that the elaboration of vitamin B_1 takes place in this region of the intestine.

In his summary of this work Dutcher [23] added: "Dextrin, on the other hand, is digested and assimilated at a slower rate, with the result that this carbohydrate reaches the cecum, where organisms (probably yeasts) have an opportunity to multiply. These organisms synthesize the B_1 and G complex, which is not readily assimilated in the lower bowel but is voided in the feces. Lactose occupies an intermediate position between the soluble sugars and dextrin."

Dutcher mentioned yeasts as possible organisms in this connection, but Shimoda [24] reported Bacillus coli as having been proved in his experiments to be able to synthesize vitamin B_1. In this explanation of the results yielded by the trials with different carbohydrates, it is assumed that synthesized vitamin B_1 is thrown out into the semifluid chyme and thus made available for absorption. In some unpublished experiments Weinstein and I grew pure cultures of organisms supplied by Bechdel and reputed to be capable of synthesizing vitamin B_1. Biologic tests of such material for B_1 content led to the conclusion that any vitamin present in the tested products is contained in the bacterial cells instead of being secreted into the medium by the cells. If one is permitted to generalize from this conclusion, it would seem (1) that any vitamin B_1 made available to the host by bacterial action within the large intestine must arise from dead and decomposed bacteria and (2) that variations in the amount of the vitamin found in the feces probably represent variations in the growth of the B_1-containing organisms.

Practically all the tests made of the feces have involved feeding of the excreta to animals, and in this case the bacterial bodies would be subjected to the action of the digestive juices secreted in the upper parts of the alimentary tract. The work of Guerrant and his associates previously cited shows that in the rat the synthesis of vitamin B_1 by micro-organisms takes place in the cecum, and for the animal to obtain the benefit of this elaboration of vitamin it must ingest the feces. On the other hand, if the vitamin could be synthesized in the small intestine by a process resulting in the presence of the vitamin in the liquid chyme outside the bodies of the synthetically active cells, the gross phenomena presented by the animals would be essentially those characteristic of refection.[25]

VITAMIN B_1 AND THE HEART

Phenomena referable to the heart have long been known as characteristic of beriberi in human beings. It is natural therefore that physiologists should be interested in the relation of vitamin B_1 to cardiac function. The most striking recent contribution to knowledge of this subject [16] is the fact that pure vitamin B_1 has no specific influence on the normal heart; only in the B_1-deficient organism does administration of the vitamin result in a demonstrable effect.

In rats subsisting on B_1-deficient diets bradycardia eventually appears, and Birch and Harris [26] have made this the basis of a technic for assay of vitamin B_1. In this connection, however, it is pertinent to point out that one cannot generalize with respect to the phenomenon of bradycardia, which undoubtedly occurs in the B_1-deficient rat. Unpublished observations by Hoff, Street and me indicate that slowing of the heart rate is not a characteristic feature of vitamin B_1 deficiency in the dog. It is true that the enlargement of the right side of the heart so characteristic of beriberi in human beings occurs with experimental B_1 deficiency produced in different species of animals, but the physiologic

18. Cowgill, G. R., and Weinstein, L.: Unpublished observations.

19. Sampson, W. L., and Keresztesy, J. C.: A Comparison of Some Methods for the Extraction of Vitamin B_1 from International Standard Acid Clay, Proc. Soc. Exper. Biol. & Med. **36:** 30-32 (Feb.) 1937.

20. Dann, Margaret, and Cowgill, G. R.: The Influence of Diarrhea on the Vitamin B Requirement, to be published.

21. Bechdel, S. I.; Honeywell, Hannah E.; Dutcher, R. A., and Knutsen, M. H.: Synthesis of Vitamin B in the Rumen of the Cow, J. Biol. Chem. **80:** 231-238 (Nov.) 1928.

22. Guerrant, N. B.; Dutcher, R. A., and Tomey, L. F.: The Effect of the Type of Carbohydrate on the Synthesis of the B Vitamins in the Digestive Tract of the Rat, J. Biol. Chem. **110:** 233-243 (June) 1935. Guerrant, N. B.; Dutcher, R. A., and Brown, R. A.: Further Studies Concerning the Formation of the B-Vitamins in the Digestive Tract of the Rat, J. Nutrition **13:** 305-313 (March) 1937.

23. Dutcher, R. A.: Recent Trends in Vitamin Research, J. Home Econ. **28:** 621-630 (Nov.) 1936; see page 629.

24. Shimoda, Y., of the Municipal Hygienic Laboratory, Osaka, Japan: personal communication to the author.

25. Bliss, Sidney, and Green, Fred: Refection in the Rat, J. Nutrition **11:** 1-19 (Jan.) 1936.

26. Birch, T. W., and Harris, L. J.: Bradycardia in the Vitamin B_1-Deficient Rat and Its Use in Vitamin B_1 Determinations, Biochem. J. **28:** 602-621, 1934.

response which this organ shows to lack of the vitamin is not the same in all species. The reader interested in this question will find an excellent summary of the facts bearing on the question of the identity of experimental vitamin B_1 deficiency with beriberi in the paper by Shimazono;[27] this author also discussed the differences in the pictures of B_1 deficiency presented by different species of animals.

Aalsmeer and Wenckebach[28] have studied the heart in cases of beriberi and advanced the suggestion that it is essentially an edematous organ. To describe the condition as hypertrophy is certainly incorrect, because the heart can return to normal size within a remarkably short time after institution of vitamin B_1 therapy. The recent observation made in Dr. A. B. Hastings' laboratory at Harvard that, in the presence of B_1 deficiency, the tissue of the auricle, in contrast to that of the ventricle, shows a marked reduction in oxygen uptake from the normal, constitutes proof that these two parts of the heart respond differently to a shortage of vitamin B_1 and that the auricle is more sensitive in this respect than the ventricle. On this basis I offer the suggestion that, because of this greater sensitivity of the auricle, this part of the heart becomes weaker, loses tone and as a result suffers greater mechanical distention in the presence of the pressure exerted by the circulating blood. If this view is correct, one should expect that administration of the vitamin would among other things restore in considerable measure the lost tone, with the result that the right side of the heart would show a prompt return to normal size. It is obvious that this cannot be the complete explanation because much of the enlargement of the right side of the heart involves the right ventricle as well as the auricles.

VITAMIN B_1 AND THE NERVOUS SYSTEM

The pathology of vitamin B_1 deficiency is treated elsewhere and therefore will not be discussed here. Let it suffice to remind the reader that polyneuritis has always been one of the striking features of beriberi in human beings and of the advanced stages of experimental vitamin B_1 deficiency. This fact has led many clinicians to test the efficacy of this vitamin in treating various conditions in which polyneuritis is a feature of the syndrome. It has been possible to show that the polyneuritis exhibited by many alcohol addicts[29] is to be attributed to lack of vitamin B_1 rather than to a specific toxic action of the alcohol on nervous tissue. Likewise, many patients with polyneuritis associated with pregnancy[30] and various clinical conditions[31] have responded favorably to vitamin B_1 therapy, which suggests that under the clinical conditions prevailing in the United States certain of the effects of vitamin B_1 deficiency have been occurring without proper recognition by the clinician. Obviously such observations as these are of great importance in relation to the question of the adequacy of the supply of vitamin B_1 to these classes of patients.

Administration of the vitamin to patients with pernicious anemia,[32] however, has had no effect on the nervous features of the disease which were due to involvement of the cord, although there was a more generalized improvement, evidenced by the patient's sense of well being and interest in food. If it is assumed that the damage to the spinal cord in these cases was irreparable, such a result is readily explained. Owing to the conflicting views[33] concerning the development of lesions of the cord as a result of specific vitamin B_1 deficiency, it is possible to take the view that administration of the vitamin should not be expected to improve the neurologic picture characteristic of pernicious anemia. Of course the patients may have been receiving a suboptimal supply of the vitamin, in which case administration of this dietary factor should result in a general improvement, which would be difficult, however, to define in precise terms.

The rotational movements frequently exhibited by animals suffering from specific vitamin B_1 deficiency suggest some lesions in the vestibular nuclei. Church[34] has offered evidence in support of this view. He has reported the discovery in the rat of perivascular hemorrhages in this region. The fact that these movements are not seen in all experimental animals suggests that the causative lesions in the brain are not of universal occurrence but instead are secondary to more fundamental tissue changes resulting from specific lack of vitamin B_1.

Church[35] has also suggested a method of vitamin B_1 assay based on his observation that B_1-deficient rats show a prolonged duration of rotary nystagmus. Although this may be true for the rat it does not appear to be the case with the dog according to my own experiments. In the latter species marked changes in the nystagmus were noticed only in the most advanced stage of B_1 deficiency and then not uniformly in all animals. Evidently there is again a failure of all species to show the same response to lack of this dietary factor. Molitor and Sampson[16] have extended this type of study to observations of the effect of large doses of the pure vitamin on the duration of nystagmus in normal rats and have observed no change.

VITAMIN B_1 AND METABOLISM

There is a wealth of evidence showing that vitamin B_1 has some role in the metabolic processes of the body. It has been shown by several investigators[36] that in the state of heightened metabolism, such as is produced experimentally by administration of thyroid, the organism's need for this dietary essential is increased. Such

27. Shimazono, J.: B-Avitaminosis und Beriberi, Ergeb. d. inn. Med. u. Kinderh. **39:** 1-68, 1931.

28. Aalsmeer, W. C., and Wenckebach, K. F.: Herz und Kreislauf bei der Beriberi-Krankheit, Berlin, Urban & Schwarzenberg, 1928.

29. Minot, G. R.; Strauss, M. B., and Cobb, Stanley: Alcoholic Neuritis: Dietary Deficiency as a Factor in Its Production, New England J. Med. **208:** 1244-1249 (June 15) 1933. Jolliffe, Norman, and Joffe, P. M.: Relation of Vitamin B (B_1) Intake to Neurological Changes in the Alcohol Addict, Proc. Soc. Exper. Biol. & Med. **32:** 1161-1162 (April) 1935. Jolliffe, Norman; Colbert, C. N., and Joffe, P. M.: Observations on the Etiologic Relationship of Vitamin B (B_1) to Polyneuritis in the Alcohol Addict, Am. J. M. Sc. **191:** 515-526 (April) 1936.

30. Plass, E. D., and Mengert, W. F.: Gestational Polyneuritis, J. A. M. A. **101:** 2020-2022 (Dec. 23) 1933. Strauss, M. B., and MacDonald, W. J.: Polyneuritis of Pregnancy, a Dietary Deficiency Disorder, J. A. M. A. **100:** 1320-1323 (April 29) 1933.

31. Wilbur, D. L., and Snell, A. M.: Deficiency States Associated with Gastro-Intestinal Disease, Tr. Am. Gastro-Enterol. A., to be published.

32. Fouts, P. J.; Kempf, G. F.; Greene, J. A., and Zerfas, L. G.: Vitamin B Intravenously for Treatment of Neurological Changes in Pernicious Anemia, J. Indiana M. A. **25:** 448-451 (Oct.) 1932.

33. Gildea, E. F.; Kattwinkel, E. E., and Castle, W. B.: Experimental Combined System Disease, New England J. Med. **202:** 523-527 (March 13) 1930. Zimmerman, H. M., and Burack, Ethel: Lesions of the Nervous System Resulting from Deficiency of the Vitamin B Complex, Arch. Path. **13:** 207-232 (Feb.) 1932.

34. Church, C. F.: Functional Studies of the Nervous System in Experimental Beriberi, Am. J. Physiol. **111:** 660-680 (April) 1935.

35. Suggested to the United States Pharmacopeia Vitamin Conference, Aug. 13, 1934.

36. Hinwich, H. E.; Goldfarb, Walter, and Cowgill, G. R.: Studies in the Physiology of Vitamins: XVII. The Effect of Thyroid Administration upon the Anorexia Characteristic of Lack of Undifferentiated Vitamin B, Am. J. Physiol. **99:** 689-695 (Feb.) 1932. Cowgill, G. R., and Palmieri, M. L.: Studies in the Physiology of Vitamins: XXII. The Effect of Experimentally Induced Hyperthyroidism on the Vitamin B Requirement of Pigeons, Am. J. Physiol. **105:** 146-150 (July) 1933. Sure, Barnett, and Smith, Margaret E.: Hyperthyroidism and Nutrition: I. Vitamin B and Thyroxin, J. Nutrition **7:** 547-555 (May) 1934.

110
938

experiments, of course, do not indicate precisely what chemical processes in the body involve this vitamin.

In his early work on this problem Funk [37] suggested that vitamin B_1 has some role in the metabolic transformation of carbohydrate in the organism. Numerous later investigators have inclined to this view. The problem has been studied in several ways. Experimental animals have been allowed to subsist on B_1-deficient diets differing markedly in content of carbohydrate, protein and fat and the time required for development of the symptoms of B_1 deficiency taken as an indication of the relation of vitamin B_1 to the metabolism of one or more of these energy-yielding foodstuffs. There appears to be little doubt that a high carbohydrate diet is much more effective in producing the symptoms of B_1 avitaminosis than one high in fat. Out of this work has come considerable discussion of the vitamin B_1-sparing action of fat. A recent example of this kind of research is seen in the paper by Westenbrink [38] in which it is reported that pigeons on a high carbohydrate diet devoid of fat had typical symptoms of B_1 deficiency in nineteen (± 4) days, whereas another group subsisting on a high fat, carbohydrate-free ration required twenty-seven (± 7) days for the symptoms to appear.

Kemmerer and Steenbock [39] endeavored to answer experimentally the question whether this B_1-sparing action of fat is due to a greater conservation of the vitamin in the tissues. Various tissues of animals subsisting on suitable experimental rations were examined for their content of the vitamin. It was found that, when a diet low in vitamin B_1 and high in fat was fed, the tissues did not contain any more vitamin than when a diet low in vitamin and also low in fat was used. From such results it would appear that one cannot explain the vitamin B_1-sparing action of fat on the basis of greater conservation of the store in the tissue of this dietary essential.

Evans and his associates [40] were able to list various natural fats according to their ability to spare vitamin B_1 and offered the suggestion that the chemical nature of the fat in some way influences its action in this regard. This idea has received considerable support from the recent work of Salmon and Goodman.[13] Like Evans and his co-workers, these investigators found that coconut fat is the most effective natural fat of those tested. More striking, however, was the observation that spastic experimental beriberi in the rat can be cured by the feeding of glyceryl caprylate or caproate. "The effectiveness of esters of single fatty acids in alleviating the symptoms of vitamin B_1 deficiency in rats depended upon the length of the carbon chain of the fatty acid. The effectiveness was maximum at the 8-carbon acid and decreased in each direction from this point." When fats and single acid esters were given with a B_1-deficient diet, the apparent nutritive value was not the same as when the diet contained adequate amounts of the vitamin.

The studies along this line appear to justify the conclusion that the function of vitamin B_1 is more likely related to carbohydrate than to fat metabolism, but the exact nature of the relationship is not evident and probably cannot be revealed by this type of experimentation. Westenbrink [41] has suggested three possible explanations: 1. When fat is fed, the organism uses in its metabolism less vitamin B_1 than it does when carbohydrate is fed. This is the view favored by Evans and his associates. 2. Whether the diet is high carbohydrate or high fat, the vitamin is used at the same rate, but the presence of much fat in some unknown manner affects the time of onset of the polyneuritis. 3. Under the two sets of dietary conditions vitamin B_1 is used at the same rate, but when carbohydrate is metabolized a toxic metabolite arises which in the absence of the vitamin is not removed and which therefore induces the polyneuritis. It will be seen that the last hypothesis constitutes a revival of the old toxin theory, with the toxin arising as a result of a "perverted intermediary metabolism" of carbohydrates.

The search for a specific function for vitamin B_1 has led many investigators to study the ability of various tissues from B_1-deficient animals to utilize oxygen or to perform certain chemical transformations which normal tissues have been shown capable of producing and which, presumably, are normal processes of intermediary metabolism. Crystallizing out of extensive investigations of this type has come the theory of Peters and his associates that vitamin B_1 functions as a co-enzyme in the metabolism of carbohydrate, more specifically in the oxidative breakdown of pyruvic acid. For a summary of the work leading to this conclusion the reader should consult the paper by Peters.[42] From the foregoing statements it is evident that two of the earlier ideas concerning the function of vitamin B_1 are supported by this theory, those relating the vitamin to carbohydrate metabolism and to biologic oxidative mechanisms.

It has long been known that lactic acid is a normal intermediate metabolite in the metabolic breakdown of dextrose. Evidence has also been available in support of the view that the lactic acid loses hydrogen under the influence of a lactate dehydrogenase with the result that the three carbon atom ketonic acid, pyruvic acid, is produced. Peters and his associates have been able to secure evidence that the cells of certain parts of the brain of the B_1-deficient pigeon show a lowered respiration in the presence of dextrose, a condition remedied by the addition of pure vitamin B_1. This action of the vitamin, on analysis, proves to be definitely that of a catalyst. Further, analysis reveals that these B_1-deficient cells, when respiring in the presence of added lactate without vitamin B_1, show an increase of pyruvate, and this increase is reduced if the vitamin is added to the in vitro system. Evidently, then, vitamin B_1 has some part in causing the disappearance of pyruvate. Study of the ratio of the extra oxygen taken up to the pyruvic acid disappearing on addition of the vitamin has revealed a value close to that yielded by the cells of normal brain tissue. On such results as these rests the contention that vitamin B_1 functions in some way to bring about oxidation of pyruvic acid. If this is correct it is obvious that in association with vitamin B_1 deficiency there should be an accumulation of pyruvic acid in the blood, and quantitative examination of this fluid for pyruvate might be made the basis of a bio-

37. Funk, Casimir: Studien über Beriberi: XI. Die Rolle der Vitamine beim Kohlenhydratstoffwechsel, Ztschr. f. physiol. Chem. **89:** 378-380, 1914.

38. Westenbrink, H. G. K.: Vitamin B-Sparing Action of Fat, Acta brev. Neerland. **3:** 95, 1933; abstr. Chem. Abstr. **28:** 7319, 1934.

39. Kemmerer, A. R., and Steenbock, Harry: A Study of the Sparing Action of Fats on the Vitamin B Content of Animal Tissues, J. Biol. Chem. **103:** 353-362 (Dec.) 1933.

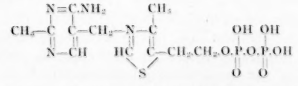
40. Evans, H. M.; Lepkovsky, Samuel, and Murphy, Elizabeth A.: The Sparing Action of Fat on Vitamin B: VII. The Effectiveness of Various Natural Fats in Sparing Vitamin B, J. Biol. Chem. **107:** 429-437 (Nov.) 1934.

41. Westenbrink, H. G. K.: Ueber den Einflusz der Menge und der Zusammenstellung der Ernahrung auf die Folgen von Vitamin B_1 Mangel, Arch. neerl. de physiol. **19:** 94-115, 1934.

42. Peters, R. A.: The Biochemical Lesion in Vitamin B_1 Deficiency, Lancet **1:** 1161 (May 23) 1936.

chemical method for detection of a state of vitamin B_1 deficiency. Platt and Lu,[43] among others, have tested this idea in cases of beriberi and observed definite increases of bisulfite-binding substances (pyruvic acid chiefly) in the blood, urine and cerebrospinal fluid. The validity of this test for B_1 deficiency obviously depends in considerable degree on the specificity of the production of pyruvate; if it can occur in association with other conditions besides vitamin B_1 deficiency its value is lessened to that extent. The observations made in cases of other disease conditions by Johnson, Meiklejohn, Passmore and Thompson[44] favor the view that the accumulation of pyruvate in the blood, urine and cerebrospinal fluid is reasonably specific for vitamin B_1 deficiency. This conclusion receives further support in the work of Thompson and Johnson,[45] who found the blood of B_1-deficient pigeons and rats to contain abnormally large amounts of bisulfite-binding substances, probably entirely pyruvic acid; in cured animals the concentration of these substances in the blood was reduced to that found in the normal organism.

It would take me too far afield to discuss carbohydrate metabolism in all its details. Let it suffice to consider the problem of the breakdown of pyruvic acid as it may be affected by vitamin B_1. Two mechanisms may be mentioned, one involving simple decarboxilation with formation of acetaldehyde and carbon dioxide and the other involving oxidation with the production of acetic acid and carbon dioxide. The first type of reaction may be brought about through the action of the enzyme carboxylase in yeast; the second chemical change occurs in the presence of a pyruvic acid oxidase. Lohmann and Schuster[46] have reported the successful isolation in pure form of the natural cocarboxylase from bottom yeast and the finding that it is essentially a diphosphoric ester of vitamin B_1. It is with particular interest therefore that the student of this problem reads the report of Stern and Hofer[47] of the synthesis of cocarboxylase from pure vitamin B_1, which synthesis has been confirmed by Lohmann,[48] who, by using pyrophosphorylchloride instead of the phosphorus oxychloride employed by Stern and Hofer, obtained much higher yields. By the work of Tauber[49] and Euler and Vestin[50] it has been shown that cocarboxylase can be produced also by enzymic synthesis. The formula of this compound, according to Lohmann, is given herewith.



Formula for cocarboxylase according to Lohmann.

There are many reasons for believing that the breakdown of pyruvic acid by decarboxylation is common in plant metabolism; whether it also occurs to a large extent in animal metabolism may be questioned. It is believed by many students of this subject that the second type of breakdown mentioned, namely, oxidation with production of acetic acid and carbon dioxide, is more likely in the animal organism. If vitamin B_1 assists in this reaction it functions also as a co-oxidase in the oxidation of pyruvic acid. Lipmann[51] has reported that such an action is exerted by Lohmann's pure cocarboxylase. Thus it appears that vitamin B_1, after phosphorylation in tissues to form a pyrophosphoric ester, can act as a coferment, assisting either the pyruvic acid carboxylase or its oxidase in breaking down this metabolite. Lipmann[51] suggested that one now has an explanation of the in vitro experiments of Peters, in which it appeared that after the addition of vitamin B_1 to the brain tissue, a substance x was converted into y, y being the true activator of pyruvic acid oxidation. It is suggested that the x of Peters is vitamin B_1 itself and the y the vitamin pyrophosphate into which it is converted by the tissue.[52]

In the discussion of the vitamin B_1-sparing action of fat, reference was made to Westenbrink's suggestion of the possibility that a toxic intermediary metabolite may be responsible for the pathologic changes characteristic of vitamin B_1 deficiency. In the light of the work just reviewed, calling attention to lactic and pyruvic acids as metabolites important in this connection, one might consider that one or the other or both of these acids can be toxic and therefore accumulation beyond a certain point be productive of injury to tissues. However, it has not been possible to induce symptoms by injections of lactate.[26] Therefore, there is little support for the view that lactic acid is the hypothetic toxic metabolite. With respect to pyruvic acid the amounts present in the blood even under conditions of accumulation have proved to be small. It is unlikely therefore that this substance can be the searched-for toxin. Peters preferred to attribute to the deficiency of vitamin an inability of cells to develop from carbohydrate sufficient energy for normal cell processes, with a resultant failure of important functions, the precise nature of the functional derangement depending on the cells involved. According to this idea it is unnecessary to postulate the presence of a toxic metabolite.

It will be noticed that this role in carbohydrate metabolism gives vitamin B_1 presumably a more or less generalized function in the body, instead of one peculiar to a given organ or group of cells. Also vitamin B_1 is placed in the category of substances involved in biologic oxidations and reductions, a group already containing numerous compounds. In view of this it may not be amiss to suggest the wisdom of suspending final judgment for the time being with respect to the universal character of the function of vitamin B_1 in all cells. May it not be that in some cells of the body the breakdown of pyruvic acid is accomplished by mechanisms other than the ones already demonstrated to involve vitamin B_1?

PHARMACOLOGY OF VITAMIN B_1

The isolation of vitamin B_1 and its synthesis have made possible the study of its pharmacologic action. Molitor and Sampson[16] have conducted such an investigation, some of the results of which have already

43. Platt, B. S., and Lu, G. D.: Chemical and Clinical Findings in Beriberi with Special Reference to Vitamin B_1 Deficiency, Quart. J. Med. **5**: 355-373 (July) 1936.

44. Johnson, R. E.; Meiklejohn, A. P.; Passmore, Reginald, and Thompson, R. H. S.: A Note on the Level of Carbonyl Compounds in Human Blood, Biochem. J. **29**: 2506-2509, 1935.

45. Thompson, R. H. S., and Johnson, R. E.: Blood Pyruvate in Vitamin B_1 Deficiency, Biochem. J. **29**: 694-700, 1935.

46. Lohmann, K., and Schuster, P.: Ueber die Co-Carboxylase, Naturwissenschaften **25**: 26, 1937.

47. Stern, K. G., and Hofer, J. W.: Synthesis of Co-Carboxylase from Vitamin B_1, Science **85**: 483-484 (May 14) 1937; Enzymologia **3**: 82-95, 1937.

48. Private communication to K. G. Stern.

49. Tauber, Henry: Enzymic Synthesis of Co-Carboxylase, Science **86**: 180 (Aug. 20) 1937.

50. Euler, H. V., and Vestin, R.: Enzymatische Synthese von Cocarboxylase mit Vitamin B_1 und Phosphat, Naturwissenschaften **25**: 416, 1937.

51. Lipmann, Fritz: Pyruvic Acid Dehydrogenation, Vitamin B_1 and Cocarboxylase, Nature **140**: 25 (July 3) 1937.

52. A more extended discussion of this subject was given by Williams, R. R.: The Chemistry of Thiamin (Vitamin B_1), J. A. M. A. **110**: 727 (March 5) 1938.

been cited. An additional conclusion of interest is that pure vitamin B_1 increases the oxygen consumption only in the B_1-deficient animal. Relatively enormous doses are without effect in the normal organism. All the pharmacologic tests of this substance yielded essentially the same conclusion: Vitamin B_1 exerts a demonstrable action only in the B_1-deficient animal. As no toxic symptoms of any kind were observed when doses approximating 25,000 or more times the estimated daily requirement were administered, it is evident that this dietary essential now available in pure form for clinical use is not to be regarded as a drug physiologically active within a certain range of dosage and dangerous to use when this range is exceeded. Instead, it is to be considered a normal and necessary part of the organism which exerts its function whenever it is needed, and any excess of supply beyond a modest amount capable of storage in the tissues for a relatively short period is eliminated through the kidneys. It is readily absorbed whether given by mouth or parenterally. With this vitamin now available in pure form and methods being perfected for its chemical determination, it is not unlikely that the future will soon see the abandonment of various "units" by which to express its activity, in favor of the use of definite dosages of the pure substance.

REPORT ON POTENCY OF LIVER PRODUCTS

BY THE UNITED STATES PHARMACOPEIA ANTI-ANEMIA PREPARATIONS ADVISORY BOARD

The standardization of products for the treatment of pernicious anemia is defined for the first time by the Eleventh Revision of the United States Pharmacopeia as follows: "Liver, stomach and other preparations used for this purpose, to be recognized as meeting the specifications of this Pharmacopeia, must be approved by the 'U. S. P. Anti-Anemia Preparations Advisory Board.' Approved products must have complied with the following specifications: 1. There shall have been submitted from time to time, as requested by the board, satisfactory clinical data from treatment, with the product in question, of cases of addisonian pernicious anemia. 2. The clinical data submitted shall satisfy the U. S. P. Anti-Anemia Preparations Advisory Board that the administration of the material in question, as prepared from liver or stomach, can produce a satisfactory result in the dose given."

In accordance with this requirement, the U. S. P. Anti-Anemia Preparations Advisory Board has considered data submitted by various pharmaceutical companies. In each case the response of the patient to the liver extract in question was studied particularly with respect to the reticulocyte and red blood cell production resulting from the daily administration of a uniform amount of each preparation. The nature of the preparations submitted has been either dry liver extract (extractum hepatis), liquid extract of liver, (liquor hepatis) or parenteral solution of liver, (liquor hepatis purificatus), as defined in the Pharmacopeia of the United States, Eleventh Revision.

Because of the variation in the efficiency of different processes of manufacture, the therapeutic activity of the final product does not necessarily correspond to the amount of liver from which it is derived. It is therefore necessary to define the therapeutic activity of the final product in other terms. Accordingly, the board has assigned to each acceptable preparation a value in terms of units. The amount of material constituting a "unit" is considered to be that amount of material which, when given daily to patients with pernicious anemia, has produced a satisfactory hematopoietic response. Since in the average case material derived from about thirty times as much liver must be given by mouth to produce the same response as when given by injection, it has been necessary to define the "unit" either as an "oral" unit or as an "injectable" unit, according to the intended method of administration of each preparation.

Accordingly, it is understood that on labels, bottles or cartons, or in advertising circulars, the manufacturer whose products have been assigned unitage by the board shall no longer state the number of grams of liver employed in making the preparation but merely either the number of cubic centimeters or grams of material constituting a unit. Depending on the method to be used in the administration of the preparation, the unit will be defined as either an "oral" unit or an "injectable" unit. Definition of the number of units in a preparation for "oral" administration in terms of "injectable" units or vice versa is not permitted. It is further understood that, if any dosage is suggested by the manufacturer, the dosage recommended should not be less than one unit a day, whether given daily or at longer intervals. The wording on the label or in the package literature concerning the unitage will give the following information: "The daily {oral / intramuscular} administration of —— (no.) {grams / cc.} (capsules, teaspoons, etc.) of material prepared by the method employed in producing the contents of this {bottle / vial / package} has been demonstrated to produce a satisfactory hematopoietic response in pernicious anemia, and constitutes a unit according to the United States Pharmacopeia Anti-Anemia Preparations Advisory Board."

In general it is recommended that, without good evidence that no harm will result, the amount of material administered should probably not be less than one unit a day, whether given daily or in multiple amounts at longer intervals. In many instances it is probable that the clinical indications will render it advisable to give the patient much more than a dosage averaging a unit a day. It must be recognized that the amount of material constituting a unit is determined largely on the basis of the hematopoietic response and does not imply that such an amount is necessarily effective in the control of gastro-intestinal or neural manifestations. Furthermore, there is some evidence that the effectiveness of different types of preparations, although similar when defined in terms of units with respect to blood formation, may differ in their effectiveness on the gastro-intestinal or neural manifestations. A full discussion of the indications for the administration of liver preparations is obviously outside the scope of this announcement; and through the cooperation of the American Medical Association and the Committee of the Revision of the United States Pharmacopeia, a special article on this subject has been published: "The Use of Drugs in the Treatment of Anemia" (THE JOURNAL, Nov. 14, 1936, p. 1633).

The board will, as occasion arises, reevaluate products based on new clinical data or assign unitage to new products submitted by manufacturers and accepted by the board.

V 1
193

Council on Pharmacy and Chemistry

PRELIMINARY REPORT OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING PRELIMINARY REPORT.

PAUL NICHOLAS LEECH, Secretary.

ALLANTOIN

Recently surgical maggots were omitted from New and Nonofficial Remedies at the request of the manufacturer. Presumably, this was related to the fact that the therapeutic use of the maggots had been superseded by the use of allantoin. In 1935 one brand of allantoin was submitted to the Council at the request of an author who wished to have his article, concerning its therapeutic use, published in THE JOURNAL. However, the manufacturer (Merck & Company) stated that it was not prepared to present the product formally at that time and to date has not submitted a complete presentation.

Subsequently the National Drug Company presented its brand of allantoin in several dosage forms. More recently the firm has forwarded additional evidence consisting of summaries of letters from physicians as well as photostatic copies of some of these letters, which are similar to testimonials. The material presented is considered later in the report.

Although it had been observed for many years, and especially in war time, that wounds which had become infected with maggots healed rapidly, Baer,[1] was the first to apply maggots deliberately for the purpose of speeding the repair and healing of chronic suppurative infections. Robinson[2] referred to the reports of Baer,[1] Buchman[3] and Myers[4] as well as to his own work[5] and mentioned the many theories that had been advanced in explanation of the healing activity of maggots. It was generally presumed that the effective agent is a substance secreted by the maggots. Robinson studied the problem and described the many helpful indications which led him to the conclusion that the effective agent is allantoin. Among these were the effect of macerated embryonic tissue on wounds, the fact that embryos possess a well developed allantois which contains allantoin, that maggots like most animals probably excrete end products of purine metabolism largely as allantoin, and that the production of allantoin through the disintegration of uric acid has been said to be accelerated in an alkaline medium such as exists in the intestine of maggots.

Following this line of reasoning, Robinson examined sterile and nonsterile maggot excretions and found that they contained allantoin. He then tested the effect of allantoin derived from other sources on chronic nonhealing wounds, including ulcers and burns. It was found to be an effective agent although in certain cases of osteomyelitis the rate of healing was not as rapid as when the maggots were used initially. This he believed was to be expected, since maggots themselves not only excrete allantoin but also remove detritus and reduce the infection. Robinson, in a more recent report, described his isolation of a substance from maggots' excretions which had the property of stimulating healing in infected wounds. He identified it as allantoin and concluded that it was at least one of the more important factors contributing to the healing effects noted in maggot therapy. Robinson[6] presented an exhibit of this work at the 1936 Kansas City session of the American Medical Association.

Although the substance appeared to be something less than maggot therapy as far as its effectiveness was concerned, Robinson noted that allantoin was bland, stable, harmless, had no odor and was nonirritating. He considered it quite inexpensive and described the methods for preparing it for use and applying it to the wound.

Allantoin is not a new remedy. Macalister in 1912 noted the use of comfrey root by the natives of rural England. They applied it to wounds for the purpose of promoting healing. Macalister applied the agent experimentally and also had it chemically analyzed. He used a rather strong infusion of the comfrey root in the successful treatment of an extensive rodent ulcer of the chest which under all other methods had continued to grow more extensive. The chemical analysis which he had made resulted in the determination of the fact that the substance contained from 0.8 to 0.9 per cent of allantoin. He noted that the people of England had used the comfrey root for many centuries, but no mention was made of it in any pharmacopeia which was available to him, nor did it appear to have ever been an official drug anywhere in the world. Subsequently it has been recognized and is described in the British Pharmaceutical Codex under the name Symphytum with the synonym comfrey root. It is stated to be the dried rhizome and root of Symphytum officinale (Boragianaceae). It is stated to contain from 0.6 to 0.8 per cent of allantoin. Further, allantoin itself is a British Pharmaceutical Codex item and both preparations are described as cell proliferants in Martindale's Extra Pharmacopeia.

Bethune[7] noted the work of Macalister[8] and of Robinson[9] and studied the use of maggots and allantoin in certain tuberculous and nontuberculous suppurative lesions of the lung and pleura. Bethune pointed out the advantages of allantoin over maggot therapy but did not use it extensively in this series of cases. On the basis of the work done by Robinson and of subsequent clinical studies which are few and far between,[10] it would seem that allantoin might easily replace maggot therapy. While it may not be quite as effective an agent, the convenience, inexpensiveness and ease with which it is administered to a wound gives it a great many advantages over the use of maggots. Patients have been known to object to maggot therapy not only because of the nature of the fly but also because of its activity when placed on a wound. The question of always being certain that the surgical maggots have been properly prepared for the use in wounds and the necessity of insuring against such diseases as tetanus in the use of maggots becomes unnecessary.

About the time allantoin was being prepared for the pharmaceutical market, Robinson[11] carried his experimentation one step further and reported that a constituent derived from allantoin was probably responsible for its effectiveness. The product is urea and it is even less expensive than allantoin. Robinson reported a series of fourteen cases and found that urea was capable of stimulating healing in chronic purulent wounds and that there was a resultant cleansing of the wound by removal of necrotic material and pyogenic bacteria. He believes that this healing action probably accounts, in part, for the custom prevalent in the old world of using urine for the healing of wounds. Urea, which is manufactured in enormous quantities, is readily available.

An article appearing in THE JOURNAL, April 3, 1937, by Holder and MacKay[12] notes that Symmers and Kirk[13] more than twenty years ago used urea solutions in the dressing of wounds with excellent results, that Millar[14] used it later in sup-

1. Baer, W. S.: Sacro-Iliac Joint; Arthritis Deformans; Viable Antiseptic in Chronic Osteomyelitis, Proc. Internat. Assembly, Inter-State Post-Grad. M. A. North America (1929), **3:** 371, 1930; The Treatment of Chronic Osteomyelitis with the Maggot (Larva of the Blow Fly), J. Bone & Joint Surg. **13:** 438 (July) 1931.

2. Robinson, William: Stimulation of Healing in Nonhealing Wounds by Allantoin Occurring in Maggot Secretions and of Wide Biological Distribution, J. Bone & Joint Surg. **17:** 267 (April) 1935.

3. Buchman, Joseph, and Blair, J. E.: Maggots and Their Use in the Treatment of Chronic Osteomyelitis, Surg., Gynec. & Obst. **55:** 177 (Aug.) 1932. Buchman, Joseph: The Rationale of the Treatment of Chronic Osteomyelitis with Special Reference to Maggot Therapy, Ann. Surg. **99:** 251 (Feb.) 1934.

4. Myers, Jacob, and Czaja, L. M.: The Maggot Treatment of Osteomyelitis, Illinois M. J. **60:** 124 (Aug.) 1931.

5. Robinson, William, and Norwood, V. H.: The Role of Surgical Maggots in the Disinfection of Osteomyelitis and Other Infected Wounds, J. Bone & Joint Surg. **15:** 409 (April) 1933. Robinson, William: Literature Relating to the Use of Maggots in the Treatment of Suppurative Infections, United States Department of Agriculture, Bureau of Entomology, Circular E-310 (Revised), June 1934.

6. Robinson, William: Allantoin, a Constituent of Maggot Excretions, Stimulates Healing of Chronic Discharging Wounds, J. Parasitol. **21:** 354 (Oct.) 1935.

7. Bethune, Norman: Maggot and Allantoin Therapy in Tuberculous and Nontuberculous Suppurative Lesions of the Lung and Pleura, J. Thoracic Surg. **5:** 322 (Feb.) 1936.

8. Macalister, Charles: A New Cell Proliferant: Its Clinical Application in the Treatment of Ulcers, Boston M. & S. J. **1:** 10, 1912.

9. Robinson (footnotes 2, 5 and 6).

10. Fotheringham, W. Teierina, and Gurruchago, Juan V.: La alantoina como estimulante de la reparacion, Bol. y trab. de la Soc. de cir. de Buenos Aires **20:** 410 (June 17) 1936; La antoina en la terapeutica del proceso de reparacion, Rev. med. del Rosario **26:** 66 (Jan.) 1936. Robinson, (footnotes 2 and 6). Bethune.[7] Macalister.[8]

11. Robinson, William: Use of Urea to Stimulate Healing in Chronic Purulent Wounds, Am. J. Surg. **33:** 192 (Aug.) 1936.

12. Holder, Hall, G., and MacKay, Eaton, M.: The Use of Urea in the Treatment of Infected Wounds, J. A. M. A. **108:** 1167 (April 3) 1937.

13. Symmers, W. S., & C., and Kirk, T. S.: Urea as a Bactericide and Its Application in the Treatment of Wounds, Lancet **2:** 1237, 1915.

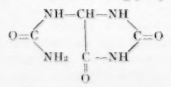
14. Millar, W. M.: Urea Crystals in Cancer, J. A. M. A. **100:** 1684 (May 27) 1933.

pressing the foul odors of sloughing cancer, and that Foulger and Foshay [15] used it in treating infected wounds of various sorts. In spite of these reports, urea has never enjoyed widespread use. The authors go on to describe a series of cases in which urea was found to be efficacious. They do not agree with Robinson that urea directly stimulates healing and it is their opinion that this is not the case in the mechanism of either maggot therapy or strong urea solutions. They attribute the effectiveness of all these forms of treatment to the removal of deterrents to healing. They suggest that thio-urea and urea-picrate may prove useful in the treatment of wounds. Kaplan [16] has recently confirmed the work of Robinson and concluded that allantoin is superior to maggot therapy in the same respects which Robinson had noted. It may be that urea and urea compounds may supersede allantoin, much as the latter is superseding maggot therapy.

In further consideration of allantoin, it is noted that there is almost a dearth of clinical reports on its use. For example, on the date of March 25, 1937, the manufacturer submitted a list of publications which have appeared in the literature on its use. The first of these is the article by Robinson [2]; the second is by Bethune [7]; the third by Rice [17]; the fourth by Greenbaum [18]; the fifth by Nicholl,[19] and the sixth by Kaplan [16] The articles by Robinson,[2] Bethune [7] and Kaplan [16] were considered as acceptable evidence in support of the presentation. The other articles were by a member of the firm's chemistry staff, a chiropodist and an osteopath. To supplement this bibliography, the firm submits a chart of physicians who have used the solution and ointment of allantoin. This consists of the name and address of the doctor, the date, the disease in which it is used, the form of allantoin used and the result obtained. These results are indicated as "very encouraging," "good," "rapid progress," "splendid," "ulcer reduced," "healed," "excellent," and so on. To support this the firm submitted six photostatic copies of letters from clinicians which give partial descriptions of cases in which they have employed allantoin. One of these, a letter from a Minnesota physician, does not even contain a reference to the use which was made of allantoin.

"This is just a note to remind you that we received the Allantoin solution and the ointment. I should like to report that while in some instances the solution seems to increase the intestinal irritability, in a few instances it seems to be definitely helpful. For my work, the solution is preferable."

The A. M. A. Chemical Laboratory has examined the National Drug Company's brand of allantoin, as well as its various dosage forms. Allantoin is glyoxyldiureid:



The Laboratory found that the standards described by the manufacturers for their product checked in detail. Briefly the dosage forms which have been submitted include the following: A bottle containing 10 Gm. of allantoin crystals which supposedly is intended to be made up into various solutions similar to the one used by Robinson,[16] and a 1½ ounce collapsible tube of an ointment containing in a greaseless base 2 per cent allantoin and 0.5 per cent chlorbutanol. (Apparently chlorbutanol replaces phenylmercuric nitrate, which was formerly used in these preparations for the purpose of rendering them sterile. The latter cannot be boiled or autoclaved without resultant chemical change.) The Laboratory has expressed the opinion that the effectiveness of allantoin must be greatly reduced in ointments, because of the large amounts of inert ingredients present. This opposes a claim made by the firm in some of its advertising literature that one of the advantages of allantoin [over maggot therapy] is "increased healing of allantoin by the special ointment base." It is also contrary to the experience of Greenbaum [18] of the firm's technical staff, who described successful use of the ointment. The evidence for the usefulness of this dosage form requires further study.

Two other dosage forms have been submitted: (1) a capsule containing 0.4 Gm. of allantoin and 0.25 Gm. of chlorbutanol, the contents of which are to be dissolved in hot water, and (2) a 3 per cent alcoholic solution of allantoin. According to a listing in the *American Druggist*, November 1936, these capsules are intended for internal administration for treatment in chronic colitis. The firm has not submitted, nor is the referee aware of, any literature on which such a recommendation could be based. However, the letter from the Minnesota physician, already quoted, may be suggestive of forthcoming evidence. Macalister, as noted in his original report on the use of the comfrey root, employed it internally in the treatment of gastric ulcer and suggested that allantoin might prove of value for that purpose. Greenbaum [18] suggests the following:

"Realizing the clinical possibilities of allantoin, we are studying the action of vegetable mucin obtained from okra combined with allantoin in colloidal dispersion for the treatment of colitis and gastric, peptic and duodenal ulcers. Allantoin with vegetable mucin combines the mechanical coating action of the powdered okra on the lining of the stomach with the healing action of allantoin on the inflamed mucosa of the stomach."

This is not sufficient evidence to warrant further consideration of this dosage form.

Greenbaum [18] also suggests that allantoin may be useful as a surgical dusting powder. An additional dosage form (not presented) is mentioned by Nicholl [19]—a nasal jelly which he claimed he used with success in certain nasal conditions.

In view of the foregoing consideration, the Council decided that further evidence for the usefulness of allantoin, and especially for the capsules, is needed. The Council, therefore, postponed consideration of allantoin and of the National Drug Company brand of allantoin, and authorized publication of this preliminary report.

15. Foulger, J. H., and Foshay, Lee: The Antiseptic and Bactericidal Action of Urea, J. Lab. & Clin. Med. **20:** 1113 (Aug.) 1935.
16. Kaplan, Theodore: Allantoin Treatment of Ulcers, J. A. M. A. **108:** 968 (March 20) 1937.
17. Rice, Eugene C.: Diabetic Ulcers and Their Treatment in Podiatry, with Special Reference to Use of Allantoin and 2 per Cent Urea, J. National Association of Chiropodists, October 1936.
18. Greenbaum, Frederick R.: Allantoin—A New Granulation Tissue Stimulating Substance with Especial Emphasis on Allantoin in Ointment Form, Am. J. Surg. **34:** 259 (Nov.) 1936.
19. Nicholl, Robert G.: Maggot Therapy and Allantoin, J. Am. Osteopathic A. **36:** 345 (March) 1937.

REPORTS OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

PAUL NICHOLAS LEECH, Secretary.

HYPOSOLS SULISOCOL NOT ACCEPTABLE FOR N. N. R.

Under the name Hyposols Sulisocol, The Drug Products Co., Inc., presented for the Council's consideration a preparation stated to contain 20 mg. of "Sulphur Colloid" in 2 cc. of "Autoisotonized Solution." It is claimed to be prepared by interaction in solution of sodium sulfide and sulfurous acid in the presence of dextrin. According to the directions given by the firm, the preparation is to be injected intravenously or intramuscularly. The dosage recommended by the firm involves injection of 0.002 Gm. of sulfur per dose, a very small amount, particularly when administered intramuscularly.

The manufacturer submitted a booklet of sixteen pages entitled "Colloidal Sulphur in Chronic Arthritis and Allied Conditions." This booklet embraces mainly methods for determining the cystine content, sedimentation rate and nonfilament count, with abstracts and excerpts of the literature on colloidal sulfur therapy, together with several photographs of joints involved in arthritis. There is presented a bibliography of forty references to the literature. Not all these references are important, and some of them, when actually consulted, are rather damaging to the firm's claims for Hyposols Sulisocol. For example, the bibliography includes two papers by R. L. Cecil (THE JOURNAL, April 22, 1933, p. 1220; Nov. 24, 1934, p. 1583). In neither paper does Cecil mention the use of sulfur; on the contrary, he says (p. 1227):

"Drugs can quickly be dismissed. Iron for the anemia, arsenic and strychnine for their tonic effects, the salicylates to ease the pain—that about covers it. Gold thiocyanate has been advocated abroad but has been disappointing in my hands."

The second paper of Cecil's is one of a symposium in which Irons and Swaim participated, neither of whom recommended the use of sulfur. One of the papers cited, that of Steinbrocker and Hartung (THE JOURNAL, March 4, 1933, p. 654),

is not concerned with treatment. Senturia (*J. Bone & Joint Surg.*, **16**:119 [Jan.] 1934), Sullivan and Hess (*ibid.*, p. 185) and Wheeldon and Main (*ibid.* **15**:94 [Jan.] 1933) recommend the use of another commercial colloidal sulfur. None of the papers that the Council's referee examined deal with the preparation of the Drug Products Co., and it is stated in the firm's booklet that the soluble colloidal sulfur is an original product, not an imitation. It might be assumed that, if colloidal sulfur were useful in the treatment of arthritis, this preparation would also be useful; but if "an original product" means anything, it means it is different from all others.

Since the therapeutic treatment of arthritis is highly specialized, the Council requested the assistance of a clinician who is engaged in a large hospital clinic devoted mainly to the study of arthritis. The consultant gave the following opinion:

> Colloidal sulfur, as well as several other drugs, has been advocated during many years of the last several decades for the cure of arthritic conditions. None of them to date have become established. The reports concerning the use of colloidal sulfur in arthritis, in the opinion of your consultant, are inadequate. It is significant that the larger, recognized clinics have not reported on the use of this preparation. As far as the consultant can find, none of the authors reporting on colloidal sulfur have used adequate criteria of improvement noted in patients. In the consultant's opinion, the value of colloidal sulfur in the treatment of arthritis has not, to date, been established.

Another specialist in the study of arthritis expressed to the Council's referee verbally a view in harmony with that just stated.

The Council declared Hyposols Sulisocol not acceptable for New and Nonofficial Remedies because of lack of evidence of its therapeutic value (conflict with rule 6), since such products have been in use for many years without having their therapeutic value recognized by the leaders in medicine who are concerned with the treatment of arthritis.

When the foregoing report was submitted to the firm in accordance with the Council's custom, a lengthy correspondence ensued. The firm, however, submitted no argument or evidence to change the Council's decision as to the unacceptability of the product. The firm implied that there was misrepresentation in the statement that Dr. Senturia did not use Sulisocol. In the paper referred to (published in 1934) Dr. Senturia definitely states that he used a certain other colloidal sulfur preparation. From correspondence with the firm and with Dr. Senturia it appears that the latter arranged to use Sulisocol in the summer of 1936, but no report on such work had been submitted to the Council. The product is meanwhile being actively promoted, and the Council felt obliged to publish its report for the information of the medical profession.

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

SULFANILAMIDE (See Revised Supplement to New and Nonofficial Remedies, 1937, p. 27).

Sulfanilamide-Abbott.—A brand of sulfanilamide-N. N. R.

Manufactured by the Abbott Laboratories, North Chicago, Ill. No U. S. patent or trademark.

Sulfanilamide Tablets, 5 grains.
Sulfanilamide Tablets, 7½ grains.

METRAZOL (See New and Nonofficial Remedies, 1937, p. 301).

The following dosage form has been accepted:

Metrazol Sterile Aqueous Solution, 10 per cent: A sterile aqueous solution containing metrazol 0.1 Gm. per cubic centimeter, for parenteral injection.

PROCAINE HYDROCHLORIDE-SQUIBB (See New and Nonofficial Remedies, 1937, p. 70).

The following dosage form has been accepted:

Ampule Sterile Solution Procaine Hydrochloride-Squibb 10 per cent, 2 cc.: Each cubic centimeter contains procaine hydrochloride-U. S. P. 0.1 Gm. in sterile distilled water.

Manufactured by E. R. Squibb & Sons, New York. No U. S. patent or trademark.

Council on Foods

ACCEPTED FOODS

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COUNCIL ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION AND WILL BE LISTED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED.

FRANKLIN C. BING, Secretary.

GARTH BRAND GRAPEFRUIT JUICE, SWEETENED AND UNSWEETENED

Manufacturer.—Tyrrell and Garth, Houston, Texas.

Description.—Canned grapefruit juice (1) unsweetened and and (2) with added sucrose, retaining in high degree the natural vitamin C content.

Manufacture.—Carefully inspected grapefruit is thoroughly cleaned, again inspected, cut in half, and reamed. The resulting juice is strained, tested for sugar with the Brix hydrometer and, if sufficiently concentrated (approximately 11° Brix), is pasteurized, automatically filled into cans, and sealed. If the strained juice does not contain the desired amount of sugar, sucrose is added and the juice is then pasteurized, filled into cans and sealed.

Analysis (submitted by manufacturer).—(1) Unsweetened: moisture 90.1%, total solids 9.9%, ash 0.32%, fat (ether extract) 0.1%, protein (N × 6.25) 0.5%, sucrose 2.0%, invert sugar 6.7%, crude fiber 0.03%, carbohydrate other than crude fiber (by difference) 8.9%. (2) With added sucrose: moisture 89.2%, total solids 10.8%, ash 0.31%, fat (ether extract) 0.1%, protein (N × 6.25) 0.5%, sucrose 2.1%, invert sugar 7.4%, crude fiber 0.03%, carbohydrate other than crude fiber (by difference) 9.9%.

Calories.—0.4 per gram; 11 per ounce.

Vitamins.—As determined by chemical titration with 2-6 dichlorophenolindophenol the sweetened juice contains 0.29 mg. of vitamin C per cubic centimeter and the unsweetened juice 0.32 mg. per cubic centimeter. Both juices therefore contain approximately 600 International units of vitamin C per hundred cubic centimeters; 180 International units of vitamin C per fluidounce.

MAYTIME BRAND EVAPORATED MILK

Manufacturer.—Dairy Belt Milk Products Company (also known as Dairy Belt Cheese and Butter Company), Spencer, Wis.

Description.—Unsweetened, sterilized evaporated milk.

Manufacture.—Milk from company inspected farms is tested, preheated, evaporated under vacuum, homogenized, cooled, filled into cans, sealed and sterilized.

Analysis (submitted by manufacturer).—Moisture 73.8%, total solids 26.2%, ash 1.5%, fat (ether extract) 8.0%, protein (N × 6.25) 6.5%, lactose (by difference) 10.2%.

Calories.—1.4 per gram; 40 per ounce.

SEXTON BRAND LIMA BEANS, WATER PACKED

Manufacturer.—John Sexton & Company, Chicago.

Description.—Canned lima beans, packed in water.

Manufacture.—Lima bean vines are thrashed, beans mechanically cleaned and hand sorted, white beans discarded, green beans graded, blanched, washed, inspected, mechanically filled into cans, hot water added, sealed and processed.

Analysis (submitted by manufacturer).—(Analysis of entire content including liquid): moisture 82.1%, total solids 17.9%, ash 0.79%, fat (ether extract) 0.4%, protein (N × 6.25) 3.6%, crude fiber 1.26%, carbohydrates other than crude fiber (by difference) 11.8%.

Calories.—0.65 per gram; 18 per ounce.

Claims of Manufacturer.—Choice quality lima beans packed in water without added sugar or salt. For use in special diets in which sugar or salt is proscribed or in quantitative diets of calculated composition.

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SATURDAY, MARCH 12, 1938

PYLEPHLEBITIS COMPLICATING APPENDICITIS

Pylephlebitis as a cause of mortality in acute appendicitis receives but scant mention in recent statistics. The severe pathologic conditions of the appendix and the surrounding structures, which constitute as a rule the necessary antecedents for thrombotic infection of the portal vein, are seldom observed in the early operations for acute appendicitis which are the rule today. Because of the generally fatal character of this complication if left untreated, it should not, however, be entirely disregarded in considering the mortality of acute appendicitis.

The postmortem statistics of the earlier investigators (Fitz, Armstrong) indicate that the incidence of pylephlebitis and liver abscess in patients who died from appendicitis varied from 3 to 5 per cent. According to Colp,[1] among 2,841 patients admitted to Mount Sinai Hospital of New York between 1916 and 1925 the diagnosis of pylephlebitis of appendicular origin was made nine times (about 0.3 per cent). In a more recent study Hawkes [2] stated that among 1,463 consecutive cases of all types of appendicitis covering a ten year period at the Newark City Hospital there were twelve cases with four deaths.

The thrombosis begins in the small veins of the mesentery of the appendix and extends by continuity into the ileocolic vein, which in turn communicates with the superior mesenteric, one of the main branches of the portal vein. The infected thrombi thus gain the intrahepatic radicles and cause multiple liver abscesses. Embolic transport of infected thrombi from the small radicles of the portal system may reach the liver without necessarily involving the larger venous trunks. The accompanying pathologic appearance includes, as a rule, an acutely inflamed, frequently gangrenous appendix with a much thickened, friable mesenteriolum, edema of the retroperitoneal tissues, a localized abscess and more or less extensive peritonitis.

The symptoms of pylephlebitis were clearly understood and well described by pioneer workers. Thus Deaver wrote in 1909: "The pylephlebitis is sometimes of the mild or noninfectious variety; frequently, however, the process is infectious; the thrombus becomes purulent and leads first to abscess of the liver and subsequently to general infection with pyemia. Chills are a rather uncommon occurrence in appendicitis, yet if at the onset of the attack they occur in rapid succession and are accompanied by temperature they indicate a rapidly developing gangrene of the appendix. Chills occurring on the second or third day of the attack and associated with a high fever usually indicate the development of metastatic or embolic abscesses." Kelly states that "chills are exceptional in cases of simple diffuse inflammation but are not rare with severe lesions. Of the patients with acute appendicitis not associated with abscesses or general peritonitis admitted to Johns Hopkins hospitals, 15 per cent gave a history of chills, and in all of these the appendix was gangrenous, perforated or distended with pus. Repeated chills occurring later in the course of the malady generally indicate a dissemination of the pyemic process."

The most significant symptom is the occurrence of chills followed by high temperature. Slight jaundice may develop and the liver may be enlarged and tender. There is irregular, severe abdominal pain, anorexia, signs of a profound toxemia, and death supervening in the course of two or three weeks. Thalhimer [3] emphasizes that a chill during an attack of appendicitis occurring before the operation is just as indicative of pylephlebitis as a postoperative chill. Blood cultures are as a rule negative. One of the functions of the liver is to destroy the bacteria brought to it by the portal vein. According to Thalhimer, the blood cultures will be positive only when the liver abscesses cause an infective thrombophlebitis of the branches of the hepatic veins. Bacteria then appear in the general circulation, for the lungs do not act as an efficient filter.

From a diagnostic point of view the occurrence of chills in the presence of symptoms and signs of acute appendicitis has often led to confusion and to delay of the operation, thus further minimizing the patient's chance of recovery. The early operation is undoubtedly the best prophylaxis against the occurrence of this grave complication. If all patients with acute appendicitis were operated on within the first twenty-four hours, this complication would not be seen at all. Wilms [4] in 1907 was the first to intervene successfully in a case of postoperative pylephlebitis. Drawing an analogy from Trendelenburg's ligation of the ovarian vein in puerperal sepsis, Wilms sought to prevent the extension of the thrombotic process by ligation of the veins

1. Colp, Ralph: Pylephlebitis of Appendicular Origin, Surg., Gynec. & Obst. **43**: 627 (Nov.) 1926.

2. Hawkes, S. Z.: Thrombophlebitis of the Appendicial Vein Complicating Acute Appendicitis, Surg., Gynec. & Obst. **66**: 62 (Jan.) 1938.

3. Thalhimer, William: Chills Occurring Early in Appendicitis Before Operation and Their Indication of an Operable Stage of Pylephlebitis, Arch. Surg. **8**: 658 (March) 1924.

4. Wilms: Venenunterbindung bei eitriger Pfortaderthrombose nach Appendicitis, Zentralbl. f. Chir., July 24, 1909, p. 1041.

of the ileocolic angle. The operative procedure consisted of freeing the cecum and the first coil of the ileum from the posterior parietal wall and incising the anterior leaf of the mesentery, thus exposing the vessels contained within it. The veins were ligated in two bundles, and two small arteries, which were visualized were spared. The patient made an uneventful recovery. Further experiences with the Wilms operation demonstrated, however, that it was not nearly as efficient in preventing the extension of the thrombotic process as the ligation of the jugular vein in sinus thrombosis of otitic origin or the ligation of the ovarian vein in puerperal sepsis. The difference is due to the fact that in the diseases mentioned it is possible to ligate the main venous trunk representing the chief route for the transport of thrombi, while in the case of acute appendicitis it becomes necessary to ligate the small radicles in the vicinity of the disease focus before they form a venous trunk. The ligation for that reason is often done too late, the thrombi having extended beyond the point of ligation. A further disadvantage was the fact that ligation of the vessels close to the intestine caused nutritive disturbances in the intestinal wall. It therefore occurred to Braun [5] that the ligation should be performed at the junction of the ileocolic vein with the superior mesenteric. The veins of the mesenteriolum and of the cecum merge into a fairly large single trunk, the ileocolic vein. This is joined by the right colic vein from above, but otherwise the vein has no tributaries. The trunk is not difficult to recognize and it presents no difficulties in ligation. The course of the ileocolic vein follows an oblique line from the ileocecal angle upward and mediad directly beneath the anterior leaf of the mesocolon. It can be easily followed after incision of the peritoneal covering up to the junction with the superior mesenteric vein. According to Braun, the ileocolic vein is the principal if not the only path for the transport of thrombi in appendicitis. In four necropsies studied by Braun, the thrombi were found in the radicles of the ileocolic vein alone, the other branches of the superior mesenteric vein being free of thrombi. He therefore feels that timely ligation of the ileocolic vein close to its confluence with the superior mesenteric vein would have saved the lives of these patients. The advantages of Braun's operation over that of Wilms is that the former is easier to perform, that it obviates the necessity of freeing the cecum and the ascending colon from the posterior abdominal wall, and that ligation is performed farther from the disease focus. Braun successfully operated by this method in two cases. He concludes that ligation of the ileocolic vein is indicated in every case of acute or chronic appendicitis in which symptoms of septic thrombosis of the liver are present.

It is doubtful that surgical intervention can accomplish anything once the infectious thrombotic process has passed beyond the junction of the ileocolic vein with the superior mesenteric. Neuhof's suggestion of the feasibility of gradual ligation of the portal vein is not likely to be accepted. Colp [1] reported three cases in which the portal vein and one in which the superior mesenteric were ligated. All four patients survived the shock of the operation but died of sepsis caused by liver abscess.

5. Braun, H.: Die Unterbindung der Vena ileocolica bei mesenterialer Pyämie nach Appendicitis, Beitr. z. klin. Chir. **86**: 314, 1913.

MAX BRÖDEL AND MEDICAL ILLUSTRATION

Since the time when the birth of one of Cleopatra's children was recorded in illustration on the wall of an Egyptian temple, medical art has aided an understanding of biologic and disease processes. The notebooks of Leonardo da Vinci indicate that, although an artist, he had as great a knowledge of anatomy as any other man of his time. The history of anatomic illustration shows a steady progress in the field since the middle ages. Indeed, it is sad to contemplate the day when the machine age, through its development of color photography, interior lighting of the human body and other similar methods, may relegate into obsolescence the personal craftsmanship of the biologic artist.

In 1894 Max Brödel came to Baltimore, after working on the anatomic illustrations of Spalteholz, His and Braune. The years from 1894 to 1910 saw him engaged chiefly in preparing illustrations for the works of Howard Kelly. In 1910 he became the presiding genius of a department of art as applied to medicine in the Johns Hopkins University School of Medicine. It was the only one of its kind in this country. This unique position it continues to occupy as testimony to the character of an inspired teacher. While great numbers of distinguished students have benefited from his instruction, some have been so conspicuous for their talent and skill that their names are already recognized throughout the medical world. Elizabeth Brödel of the Woman's Clinic in the New York Hospital, James F. Didusch of the Department of Embryology in the Carnegie Institution, Dorcas Hager, whose illustrations of Dr. Walter Dandy's notable surgery of the brain in Johns Hopkins University have done much to advance that difficult field, and Willard C. Shepard of Chicago are names of Brödel's distinguished pupils frequently encountered in the best medical literature of our day. His other distinguished pupils are found carrying the skill of their teacher from coast to coast. Among the institutions which have benefited by their contributions are the Wilmer, Brady, Mayo and Lahey clinics, the American Museum of Natural History, and Yale, Minnesota, Rochester, Toronto and Tulane universities.

And there are free lances who make it possible for individual physicians and investigators not connected with any formal institution to avail themselves of this type of masterful interpretation of conditions seen and procedures carried out in the laboratory and the clinic.

What a triumph for Max Brödel—to cast his eye over our medical world and to see the impress that he has made on it.

To list the innumerable books and periodicals which carry the contributions of Max Brödel and his pupils would be impossible. In some instances the Brödel pictures have been as potent as the author's description in extending a new concept to the medical profession. Could anything be more graphic than his colored illustration of Cullen's sign—that warning of abdominal hemorrhage—so perfectly portrayed as to fix itself indelibly in the mind of the medical reader, making prompt recognition of the condition possible and, no doubt, saving the lives of many people? Dr. George H. Simmons, an editor not much given to enthusiasm or raptures, used to glow in the contemplation of Max Brödel illustrations for a scientific paper that was not quite so good and accept the paper more for the pictures than for the value of the text.

The craftsmanship of Brödel and his pupils has done much to raise the standard of American medical publication. The Johns Hopkins University School of Medicine has been fortunate indeed in its professor of art in medicine; the faculty and the students have had the intimate advantage of his personal inspiration; the medical world appreciates the helpfulness of his graphic teaching. Elsewhere in this issue [1] appears a description of the presentation of his portrait to Johns Hopkins University School of Medicine. It is fitting that this portrait, from which there gazes forth the humor, the human kindliness, the scientific spirit and the artistry of this great scholar, should hang in the halls of this noted university beside those other unique masters in the medical corridors of time—Osler, Halsted, Kelly and Welch.

Current Comment

ACCIDENTS IN 1937

In a press release from the National Safety Council, the toll of accidental deaths and injuries for 1937 has been given as dead 106,000, permanently injured 375,000 and temporarily injured 9,400,000. The estimated cost of this civil carnage was $3,700,000,000. While the deaths from accidents of all causes decreased 4 per cent from 1936, traffic accidents increased 4 per cent, home accidents decreased 15 per cent, occupational accidents increased 6 per cent and public nontraffic accidents decreased 5 per cent. Although two major disasters occurred in 1937—the New London, Texas, school house explosion, in which 294 children lost their lives, and the Hindenburg disaster, in which thirty-five passengers and members of the crew were killed—the total effect was relatively insignificant in comparison with the accidental deaths occurring singly or in twos. Falls again effected more accidental deaths than any other one cause except traffic accidents. The traffic death rate per hundred thousand of population in 1937 was 30.7, compared to 29.7 in 1936, and represents a rate 62 per cent higher than 1925 and 30 per cent higher than 1933. On a mileage basis, however, the motor vehicle death rate declined from 16.6 deaths per hundred million miles in 1936 to 15.9 in 1937. Of further slight encouragement is the fact that in 1937 twenty states cut their death toll from traffic accidents, and in all but one (based on ten months' information) this was accomplished in the face of increased highway traffic. Accompanying other significant figures is the information that fifty persons were killed in 1937 in accidents involving airplanes in scheduled domestic operations. In 1936 the total was sixty-one. Forty airplane passengers were killed, as compared with forty-four in 1936. Passenger miles flown in 1937 totaled 480,000,000, resulting in a passenger death rate of 8.3 per hundred million miles, or about half that from automobile traffic accidents on a passenger mileage basis! The publicity accorded to the former throws into sharp relief the necessity for continued efforts on the still relatively unpublicized hazards of ground traffic.

AID TO THE BLIND

Thirty-six states are now cooperating with the Social Security Board in granting financial assistance to the needy blind.[1] The state with the largest number of persons receiving such assistance in July 1937 was Pennsylvania, with 10,511 receiving aid. Maine, however, was rendering aid to 137 per hundred thousand of population, as compared with 104 per hundred thousand of population in Pennsylvania. New York's 18 per hundred thousand and North Carolina's 14 were at the other end of the scale. At the New York meeting of the Academy of Ophthalmology and Otolaryngology the Social Security Board informed the council of the academy of its attempt to set up a definition of blindness to be placed before the several state agencies administering the various blind assistance laws. It is based on the definition of economic blindness proposed by the American Medical Association in 1934 and differs but little from that definition: "In general, central visual acuity of 20/200 or less in the better eye with proper correction has been considered as economic blindness. An individual with central visual acuity of more than 20/200 in the better eye with proper correction is usually not considered blind, unless there is a field defect in which the peripheral field has contracted to such an extent that the widest diameter of the remaining visual field subtends an angular distance no greater than 20 degrees." So far, however, only four states have followed the recommendation of the council and the Social Security Board in fixing a definite value to the contracted visual fields for determining blindness. Naturally the medical determination of blindness is an important point in any state program of financial aid to the blind. The council of the academy in 1936 said, in reply to the question as to who should determine the fact of blindness, "They shall be certified ophthalmologists in a given state. Or in case

1. General News, this issue, p. 823.

1. Rice, C. E.: Report to Committee of American Academy of Ophthalmology and Otolaryngology, U. S. Public Health Service.

a certified ophthalmologist is not available, then the state medical society should recommend a list of competent ophthalmologists in the state." At present only four states indicate that ophthalmologists are chosen by the state medical society. In one, the state health department chooses the examiners; in another, those listed in the American Medical Directory as practicing ophthalmologists or as eye, ear, nose and throat specialists are designated. Only one state (Maryland) has limited examiners to ophthalmologists certified by the American Board of Ophthalmology. Thirteen states have appointed supervising or consulting ophthalmologists. This variation is obviously unsatisfactory. In twenty-three of the thirty-six states there is a statutory provision that the state agency concerned with assistance to the blind (usually the state welfare board) can provide treatment for needy persons either for restoration of vision or to prevent blindness. In three additional states such provision is made through rule and regulation. A serious difficulty encountered is the confusion of terminology. The Committee on Statistics of the Blind, however, organized about 1930 at the instigation of the Census Bureau and under the auspices of the National Society for the Prevention of Blindness and the American Foundation for the Blind, has proposed a classification which has been submitted to the council of the American Academy of Ophthalmology for careful revision.

110
938

MULTIPLE ANTIGEN SENSITIVITY

Simultaneous hypersensitivity to more than one antigenic substance has been generally recognized. The toleration of one antigen without allergic manifestations has been considered a distinct probability. It has been assumed also, however, that the addition of a further specific excitant under these circumstances would lead to the production of allergic symptoms by way of a summation effect. In a recent attempt to test the validity of this hypothesis, Pratt[1] sensitized guinea pigs to two antigens in a uniform manner. Recrystallized egg albumin and horse serum globulin, both dissolved in physiologic solution of sodium chloride, were the substances given. One third were then shocked with a dosage of the first antigen, which would produce an occasional anaphylactic death, one third with a similar dosage of the second antigen, and the last third with the two antigens, given simultaneously, in a dosage represented by the sum of the individual doses given the first two groups. The degree of shock was classified from one to five plus. Seventy-three carefully selected guinea pigs were used in the experiments. The results were clear cut. If a guinea pig is specifically sensitive to two substances and is shocked with both he will react no more vigorously than he would to either one alone, provided the two antigens are equally capable of producing moderate shock. If, however, the dosage of either antigen is doubled, the animals respond with an enhanced degree of shock. The explanation for this phenomenon is not clear. It is possible, Pratt points out, that the body can react to only one antigen at a time during the short period that an anaphylactic action is taking place. Another possible explanation is that the egg albumin molecule, with a much smaller molecular weight than the horse serum globulin, is capable of leaving the vascular bed and coming into contact with the sensitized cells more quickly. As pointed out in the discussion of this paper, if these conclusions apply to man a new idea will be introduced into the practice of allergy; namely, that summation of effects from combined sensitizations may not occur to the extent previously assumed. This possibility, however, is by no means certain in view of the probably more highly sensitive and reactive nature of the guinea pig.

1. Pratt, H. N.: Anaphylaxis in Multiple Sensitive Guinea Pigs, J Allergy 9:14 (Nov.) 1937.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Society News.—Dr. Andrew Richard Bliss Jr., Memphis, Tenn., discussed socialized medicine before the Walker County Medical Society in Jasper February 11.——Dr. Dowlen D. Cox, Sheffield, discussed diseases of the kidneys at a meeting of the Franklin County Medical Society in Russellville January 4.

New District Health Unit.—The counties of Bullock, Chambers, Lee, Macon, Randolph, Russell and Tallapoosa have joined to form a new district health unit in eastern Alabama, with headquarters in Opelika. Dr. Arthur H. Graham is the medical director. According to the newspapers, the Rockefeller Foundation is cooperating with the state in supplying funds for the work, which will include a program for control of tuberculosis in an area without proper hospital facilities.

ARKANSAS

New District Health Unit.—A new district health unit has been organized for Bradley, Cleveland and Lincoln counties, with headquarters in Warren, effective January 1. Dr. Jennings Bryan Ivy has been placed in charge.

New Professor of Obstetrics.—Dr. Ernest H. White, associate professor of obstetrics and gynecology, University of Arkansas School of Medicine, Little Rock, has been appointed professor, succeeding the late Dr. Shelbey B. Hinkle. Dr. White graduated at the Harvard University Medical School in 1922 and for several years has been secretary of the Pulaski County Medical Society. He has been connected with the Arkansas school since 1923.

CALIFORNIA

Personal.—The Distinguished Achievement Award of Pi Kappa Alpha was presented to Dr. John C. Ruddock, associate clinical professor of medicine, University of Southern California School of Medicine, Los Angeles, at the fraternity's seventieth anniversary dinner in Chicago March 1.——Dr. John B. Saunders, associate professor of anatomy, University of California Medical School, San Francisco, has been appointed an editor for *Isis*, quarterly journal of the International Society of the History of Science.

Alumni Honor Memory of Dr. Kerr.—The annual alumni day program of the University of California Medical School, San Francisco, will be presented on March 22 by the William Watt Kerr Club in honor of the late Dr. Kerr, formerly professor of medicine. The morning session will be given over to clinics; speakers in the afternoon will include:

Dr. Sidney Olsen, class of 1919, The Role of the Double Ureter.
Dr. Philip H. Arnot, class of 1920, Cesarean Section.
Dr. Irvin H. Betts, class of 1915, The Doctor in General Practice.
Dr. Hiram E. Miller, class of 1917, Chronic Granuloma of Industrial Origin.

Dr. Langley Porter, dean of the medical school, will deliver the Alpha Omega Alpha Lecture to conclude the day's program.

COLORADO

Changes at the University of Colorado.—Recent changes at the University of Colorado School of Medicine, Denver, include the following:

Dr. Philip Work, to professor of neurology and head of the department.
Dr. Constantine F. Kemper, associate professor of medicine.
Dr. Harry Gauss, assistant professor of medicine.
Dr. Edward L. Harvey, assistant professor of obstetrics and gynecology.
Dr. Harold L. Hickey, assistant professor of otolaryngology.

Howard J. Shaughnessy, Ph.D., former assistant professor of bacteriology and public health, University of Illinois College of Medicine, has been appointed associate professor of bacteriology and public health to fill the vacancy occasioned by the retirement of Severance Burrage, Ph.D.

CONNECTICUT

New Superintendent of New Haven Hospital.—James A. Hamilton, superintendent of the Cleveland City Hospital, Cleveland, has been appointed superintendent of the New Haven Hospital, New Haven, effective September 1. He succeeds Albert W. Buck, Ph.D., who became head of the Charlotte Hungerford Hospital, Torrington, January 1. Mr. Hamilton graduated from Dartmouth College in 1922 and obtained his master's degree in 1923 from the Tuck Business School. He was assistant professor of industrial management at Dartmouth from 1923 to 1936 and for ten years superintendent of the Mary Hitchcock Memorial Hospital at Hanover.

FLORIDA

Directory of Florida Physicians.—The publication of a medical directory for physicians licensed to practice medicine in Florida was approved by the executive committee of the state medical society at its meeting in Tampa in January. On February 8, in Jacksonville, the state board of health unanimously endorsed the directory and the state board of medical examiners has approved the project. It is hoped to have the directory in the mail before the state medical meeting in May. The first section will contain the names and addresses of the members of the state medical association by component societies, the second the names of physicians licensed to practice medicine in Florida by cities, the third an alphabetical list of physicians licensed to practice in the state. The use of certain type and symbols will show the status of the physician. The price of the first edition will be $1.

GEORGIA

The Block Memorial Lecture.—Dr. Israel S. Wechsler, New York, delivered the fourth E. Bates Block Memorial Lecture before the Fulton County Medical Society February 24, on "Abdominal Syndromes in Diseases of the Brain."

New County Health Departments.—The state department of health announced in its January bulletin that health departments were to begin in several counties during January. Health commissioners have been appointed as follows:

Bleckley County, Dr. Henry T. Adkins, Cochran.
Bulloch County, Dr. Harry E. McTyre, Savannah.
Coffee County, Dr. Roy L. Johnson, Atlanta.
Dodge County, Dr. Johnnie L. Gallemore, Macon.
Walton County, Dr. John L. Dorough, Monroe.

Units will begin in Crisp and Monroe counties as soon as health commissioners can be secured, it was stated. Dr. Rufus Floyd Payne, Tifton, has resigned as health commissioner of Tift County to become assistant director of county health work of the state department of public health. Dr. Robert H. Haralson Jr., Atlanta, will succeed him in Tift County.

ILLINOIS

Society News.—Dr. Willis S. Lemon, Rochester, Minn., will discuss "The Development and Metamorphosis of the Primary Tubercle" before the Peoria City Medical Society in Peoria March 15. The society was addressed March 1 by Dr. Harry Culver, Chicago, on "Nonspecific Kidney Infections Including Their Surgical Complications."——The St. Clair County Medical Society was addressed in East St. Louis February 3 by Drs. Robinson Bosworth, East St. Louis, and Robert C. Farrier, Escanaba, Mich., on tuberculosis and public health, respectively.

Chicago

The Christian Fenger Lecture.—Dr. David J. Davis, dean and professor of pathology, University of Illinois College of Medicine, will deliver the second Christian Fenger Lecture of the Institute of Medicine and the Chicago Pathological Society at the Palmer House March 25; his subject will be "Pathology as a Basis for the Study of Health."

The Gehrmann Lectures.—Dr. Thomas M. Rivers, director, the Hospital of the Rockefeller Institute for Medical Research, New York, will deliver the Gehrmann lectures of the University of Illinois College of Medicine, March 23-25. His subjects are "Viruses and Virus Diseases"; "Cultivation of Vaccine Virus: Methods Employed, Types of Information Obtained, Jennerian Prophylaxis with Cultured Virus," and "Poliomyelitis."

Joint Gynecologic Meeting.—The Chicago Gynecological Society and the St. Louis Gynecological Society held a joint session February 19. Clinics were held at the Chicago Lying-In and Research and Educational hospitals. The following program was presented by members of the St. Louis society:

Dr. William C. Stude, Cesarean Section—An Analysis and a Discussion.
Dr. Thomas K. Brown, Results of Cultures of the Uterus at Cesarean Sections.
Dr. Melvin A. Roblee, Etiology of Cervicitis.

Carl G. Hartman, Ph.D., department of embryology, Carnegie Institution of Washington, Baltimore, delivered a lecture on "The Physiology and Control of Ovulation."

Society News.—Dr. Winthrop M. Phelps, Baltimore, discussed "The Care and Treatment of Cerebral Spastic Paralysis" before a joint meeting of the Chicago Orthopedic Society and Chicago Pediatric Society February 11.——Dr. Edward C. Holmblad, regional chief surgeon, Railway Express Agency, addressed the Chicago Society of Industrial Medicine and Surgery February 14 on "Factors Determining Compensation from the Medical Viewpoint," and Mr. Henry H. Rolfe, past president, Casualty Adjusters Association, "Compensability of Injuries from a Legal Standpoint."——The Chicago Neurological Society was addressed February 17 by Drs. Harold C. Voris and Milton H. Dresner on "Hodgkin's Disease of the Spine with Paraplegia, Complicated by Pregnancy"; Harry A. Paskind, Chicago, and Robert C. Lonergan, Evanston, Ill., "Treatment of Myotonia Congenita with Quinine"; Karl A. Menninger, Topeka, Kan., "Emotional Factors in Hypertension," and Horace W. Magoun, Ph.D., "Activation of the Heat Loss Mechanism by Localized Heating of the Brain."

IOWA

Graduate Courses.—The speakers' bureau of the state medical society will conduct five graduate courses this spring in Council Bluffs, Rockwell City, Clinton, Iowa City and Marshalltown. The course in Marshalltown began February 1 to continue on a monthly basis for eight consecutive months, with the exception of July and August. The courses in Council Bluffs and Iowa City will be given for eight weeks, while the Clinton course will close at the end of five successive meetings. The fee for the courses at Council Bluffs and Rockwell City will be $10 and a fee of $5 will be charged for the Iowa City and Clinton courses. The Marshalltown course will be conducted on an invitation basis by the Marshall, Hardin, Tama and Grundy county societies. Subjects to be covered include endocrinology and metabolism; what the general practitioner should know about the specialties; general therapeutics; some practical applications of new medical knowledge, and a university course dealing with gonorrhea, infection, headache and the malignant conditions.

Society News.—At a meeting of the Crawford County Medical Society in Denison recently Dr. Roland B. Morrison, Carroll, showed a film on surgical technics, and Dr. Payson S. Adams, Omaha, discussed "Sacral and Caudal Anesthesia."——The Dallas-Guthrie County Medical Society was addressed in Adel, January 20, by Drs. Keith W. Diddy and George Elvidge, both of Perry, on "Infections of the Hands" and "Septic Sore Throat" respectively.——Dr. Thomas L. Waring discussed "Treatment of Nonunion of Femoral Neck Fractures: An Analysis of Ninety-Three Cases" before the Johnson County Medical Society, Iowa City, January 5 and Dr. Robert L. Jackson, "Disadvantages of Protamine Insulin in the Treatment of Diabetes Mellitus in Children."——At a meeting of the Monona County Medical Society in Onawa January 11 Dr. Walter Scott, Sioux City, discussed "Fractured Spine Following Automobile Accidents."——Dr. W. Eugene Wolcott, Des Moines, addressed the Poweshiek County Medical Society in Grinnell February 1 on "Fractures of the Femur."——A special meeting of the Woodbury County Medical Society was addressed January 21 by Drs. Florian E. Schmidt, Chicago, and Carl F. Jordan, Des Moines, on "Control and Treatment of Pneumonia."——Dr. Leon Unger, Chicago, addressed the Scott County Medical Society at Davenport recently on "Eczema in Children." Dr. Disraeli W. Kobak, Chicago, discussed physical therapy before the society February 1.

V 1
193

KANSAS

Instruction in Pneumothorax Therapy. — The Kansas Medical Society's committee on control of tuberculosis announces that instruction in pneumothorax therapy is available to physicians at the state sanatorium for tuberculosis at Norton, in accordance with a plan approved by the board of administration. Physicians wishing this instruction should write to Dr. Charles F. Taylor, superintendent, to arrange a date for the physician to visit the sanatorium. All instruction and assistance will be given without cost. Dr. Taylor has recently developed an inexpensive pneumothorax machine which can be easily constructed by any physician with local mechanical assistance. This machine with the necessary instruction should enable any physician to give pneumothorax treatment, it was stated.

KENTUCKY

Society News.—The Jefferson County Medical Society is presenting a refresher course in physiology in lectures at each meeting just preceding the regular program. At the meeting February 7 Hampden C. Lawson, Ph.D., associate professor of physiology, University of Louisville School of Medicine, lectured on "Secondary Vascular Shock." Drs. Lawrence W. Nehil and R. Alexander Bate spoke on "Present Status of Collapse Therapy" and "Cancer" respectively.

Laboratory Service Expanded.—The state department of health announces that district public health laboratories have been established in Ashland, Madisonville and Paducah to facilitate communicable disease control. Specimen containers will be distributed through the branch laboratories to county health departments, which will in turn distribute the containers to individual physicians. In counties in which there is no full time health department, practicing physicians will receive containers directly from the nearest district laboratory. The new laboratories will perform only procedures that have a public health significance.

LOUISIANA

New Professor of Clinical Orthopedics.—Dr. Guy A. Caldwell, since 1923 in charge of orthopedics and fractures at Charity Hospital, Shreveport, has been appointed professor of clinical orthopedics at Tulane University of Louisiana School of Medicine, New Orleans.

MARYLAND

Public Lectures. — Dr. A. Stampar, former director of health of Yugoslavia, delivered a lecture on "International Health Work" in the De Lamar series in hygiene at Johns Hopkins University School of Hygiene and Public Health, March 3. Dr. Thomas Parran, surgeon general, U. S. Public Health Service, gave a Delta Omega lecture on "A Forward Look at National Health" at the school March 1.

Physicians and Patients in Mental Hospitals.—Thirty physicians were caring for the 7,212 insane or feebleminded patients in state institutions at the end of the last fiscal year, according to a report of the board of mental hygiene. None of the four hospitals for the insane, as distinguished from two institutions for the feebleminded, has as many as one physician to each 150 patients. Only the Eastern Shore institution at Cambridge came within the nursing standard, showing a ratio of seven patients to each attendant. Admissions for the fiscal year reached 3,722, the highest total since 1933. Nearly 65 per cent of all patients remain in the hospitals less than a year and about 18 per cent leave within one month; 49 per cent of patients who die in the institution die within a year.

MICHIGAN

Outbreak of Typhoid.—Newspapers reported an outbreak of typhoid in Muskegon County February 10, involving twenty-seven persons in thirteen families and causing three deaths. Four cases were reported in Marquette February 11. It was believed that the Marquette outbreak was caused by a carrier, but the results of the Muskegon investigation had not been announced at the time of this report.

Dr. Stevens Honored.—Dr. Rollin H. Stevens, Detroit, was guest of honor at a dinner January 28 given by the staff of Grace Hospital, the Detroit Roentgen Ray and Radium Society and the Detroit Dermatological Society, in observance of his seventieth birthday. Among other gifts Dr. Stevens received a leather bound copy of the January issue of *Radiology*, which was dedicated to him. Each guest received a reprint of the opening article in the journal, entitled "Rollin Howard Stevens, An Anniversary Chronicle of His Useful Life," by Dr. Percy Brown, Boston.

State Society Nights. — The Hillsdale County Medical Society joined with the Jackson County Medical Society this year in sponsoring its third annual "state society night" in Jackson January 18. The latter society is, according to the state medical journal, the originator of these affairs. The speakers included Dr. Henry Cook, Flint, president of the state medical society. The Kent County Medical Society held a similar program in Grand Rapids February 9 and the Lenawee County Medical Society in Adrian, February 16. A meeting in Sturgis in April is planned by the St. Joseph and Branch county medical societies.

Society News.—Dr. Walter A. Bastedo, New York, discussed "Physician and Pharmacist" at a joint meeting of the Detroit Retail Druggists Association and the Wayne County Medical Society March 7.——Dr. George W. Kosmak, New York, addressed a joint meeting of the Detroit Obstetrical and Gynecological Society and the Wayne County Medical Society, February 28, on "The Responsibility of the Medical Profession in the Movement for Birth Control."——At a meeting of the Oakland County Medical Society in Bloomfield Center March 3 Dr. William Mithoefer, Cincinnati, discussed "Reasons Why Nasal Sinus Surgery Is in Disrepute."——Dr. Lawrence Reynolds, Detroit, discussed "Roentgenologic Aspects of Dyspepsias" before the Ingham County Medical Society, Lansing, February 15.

MINNESOTA

Hospital News.—Construction has been started on the new $542,000 Wyman addition to the Abbott Hospital, Minneapolis, according to *Modern Hospital*. The new unit will be four stories high.——Dr. George R. Minot, Boston, delivered a lecture January 20 at the Mayo Clinic, Rochester, on "Some Aspects of the Etiology, Diagnosis and Treatment of Anemia." Dr. Jose Valls, professor of orthopedic surgery, National University of Buenos Aires, gave a Mayo foundation lecture February 3 on "Treatment of Fractures of the Neck of the Femur."

NEW YORK

Short Course on Heart Disease.—Dr. Wilhelm Dressler, Vienna, Austria, gave an address January 19 at the Syracuse University College of Medicine, on "Complications and Sequelae of Coronary Thrombosis." Dr. Dressler gave a series of lectures at the college for five days beginning January 20, on treatment for heart disease.

Society News.—Dr. Herbert H. Bauckus, Buffalo, addressed the Medical Society of the County of Niagara, Lockport, January 11, on "Common Skin Lesions, Their Diagnosis and Treatment."——Dr. Alfred Wachsberger, New York, addressed the Richmond County Medical Society at a meeting in Grasmere, January 12, on treatment and management of sinusitis.——Dr. Frank H. Lahey, Boston, addressed the Chemung County Medical Society, Elmira, January 5, on "Newer Clinical and Laboratory Developments in Thyroid Disease."——Dr. Cornelius P. Rhoads, New York, addressed the Medical Society of the County of Albany, February 23, on "Refractory Anemia, Nature and Treatment."——Dr. Edmund B. Spaeth, Philadelphia, addressed a joint meeting of the Syracuse Eye, Ear, Nose and Throat Club with the Syracuse Academy of Medicine, March 15, on "Ptosis and Its Correction."——Dr. Elliott P. Joslin, Boston, addressed the Utica Academy of Medicine, February 17, on "The Present Status of Diabetes in the United States."

New York City

Academy Presents Lectures for Teachers.—The New York Academy of Medicine and the Board of Education are presenting jointly a series of lectures for teachers in the public schools under the general title "The Health of the Pupil."

Gifts to Columbia.—Gifts received by Columbia University during January included the following for medical purposes:

Mrs. Winter Meade, $11,000 for construction at the Medical Center.

John and Mary R. Markle Foundation, $9,000 for research in the departments of practice of medicine and neurology.

Mrs. Brooks Emery, $2,000 for research in diseases of children.

E. R. Squibb and Sons, $1,250 for research in biologic chemistry.

Ciba Pharmaceutical Products Inc., $1,250 for research in biologic chemistry.

F. Trubee Davison, $1,200 for the F. Trubee Davison Jr., Gift Fund for the study of leukemia, lymphosarcoma and allied diseases.

Division of Tuberculosis Established.—Dr. Allen Kane, medical superintendent of the Municipal Sanatorium at Otisville, has been appointed director of a division of tuberculosis newly established in the New York City Department of Hospitals. Dr. Kane will supervise care of the tuberculous in city hospitals, promote coordination of the tuberculosis service of

the department of hospitals with that of private hospitals and perform various other duties directed toward improvement of the service. Dr. Kane graduated from Northwestern University Medical School, Chicago, in 1924.

NORTH CAROLINA

Course on Typing Pneumococci.—A course of instruction for laboratory technicians in typing of pneumococci was given at Duke University School of Medicine, Durham, during the week of January 24. Sixty-nine technicians registered. The course was presented as part of a program of pneumonia control recently undertaken by the state board of health, the Medical Society of North Carolina and other agencies. A symposium on pneumonia was presented January 28 by Drs. Wiley D. Forbus, Douglas H. Sprunt, David T. Smith, Robert J. Reeves, Frederick M. Hanes, Julian Deryl Hart and Angus M. McBryde.

NORTH DAKOTA

Changes Recommended in Public Health Services.—The Rockefeller Foundation recently completed a survey of the public health program in North Dakota which recommended various improvements. Among them were greater emphasis on enactment of standard milk ordinances in cities; responsibility of the state health department for tourist camp sanitation with provisions in the laboratory for chemical analysis of water and sewage; more conscientious enforcement of quarantine regulations; compulsory smallpox vaccination, with federal aid for free vaccine and vaccination of infants before their first birthdays; public funds for payment of physicians for treatment of patients with venereal disease; enactment of laws to require premarital examination for venereal disease.

OHIO

The First Selman Lecture.—The first lecture under the Julius J. Selman Foundation, established in memory of Dr. Selman by his friends, will be given at Mount Sinai Hospital March 14 by Dr. Albert A. Epstein, New York, on "Nephrosis."

State Board Prosecutions.—At a meeting of the State Medical Board of Ohio in Columbus January 4 the following results of prosecutions instituted by the board within recent months, among others, were reported:

Clifton Engel, Sandusky, unlicensed chiropractor, found guilty of conducting an office, fined $500 and costs; $250 was remitted on condition that objectionable practice and advertising be discontinued and that a fine of $50 for a previous offense be paid.

Mae Jerome, Ashtabula, found guilty of illegal practice, fined $500 and costs; $450 suspended on condition that she leave the state.

Richard C. Geilus, Ashtabula, found guilty of illegal practice, fined $500 and costs; $450 suspended on condition that he leave the state.

William C. De Benis, Cincinnati, unlicensed chiropractor, fined $50 and costs.

Alfonsa Balda, Columbus, illegal practice, fined $500 and costs, suspended on condition that he leave the state.

J. C. Carmell, Clarence C. Cox, Robert E. Cox, Hugh T. Pennell, James R. Couch and Bruce A. Tanner, Columbus, unlicensed napropaths, fined $200 each for illegal advertising. An appeal was filed.

Society News.—Dr. Charles F. Geschickter, Baltimore, addressed the Academy of Medicine of Cleveland, February 18, on "Diseases of the Breast."——Members of the medical section of the Industrial Commission of Ohio presented a symposium before the Toledo Academy of Medicine February 4. The speakers, all of Columbus, were Drs. Roy J. Secrest, on "Encephalography as an Aid to Diagnosis in Obscure Head Injuries"; Maurice B. Rusoff, "Evaluation of Disability"; Henry P. Worstell, "Chronic Osteo-Arthritis"; Sidney M. McCurdy, "Relationship of Workmen's Compensation to State Medicine," and Mr. J. A. Davis, attorney, "The Expert Medical Witness."——A symposium on fractures made up the program of the Mahoning County Medical Society, February 16, at a joint meeting with the Sixth Councilor District Medical Society in Youngstown. The speakers were Drs. Ralph R. Morrall, Chester S. Lowendorf, Thomas K. Golden, William D. McElroy and John R. Buchanan, all of Youngstown.——Dr. John H. J. Upham, Columbus, President of the American Medical Association, addressed a joint meeting of the Academy of Medicine of Cincinnati and the Cincinnati Dental Society, February 1, on "Present Day Economic Problems of Medicine and Dentistry." Dr. Chester M. Jones, Boston, addressed the academy, February 15, on "Edema and Ascites in Hepatic Insufficiency."

OKLAHOMA

Personal.—Dr. Thomas J. McGrath, Sayre, has been appointed health superintendent of Beckham County to succeed Dr. Henry K. Speed Jr., who resigned to become superintendent of the new Western Oklahoma Charity Hospital at Clinton.——Dr. Russell H. Lynch, Hollis, has been appointed health officer of Harmon County.

OREGON

New Health Unit.—Establishment of a health unit for Multnomah County was recently announced. Dr. William R. Hicks, formerly of Yonkers, N. Y., a graduate of Syracuse University College of Medicine in 1936, will be the health officer.

Medical Library to Be Expanded.—The University of Oregon Medical School, Portland, recently announced a gift of $100,000 from the Rockefeller Foundation for expansion of the school's library facilities. A new wing will be added to the medical school building at a cost of about $200,000, part of which will be obtained from other gifts. The new appropriation brings to $800,000 the contributions of the Rockefeller Foundation to the Portland medical center.

Jones Lectures.—Dr. Eugene M. Landis, assistant professor of medicine, University of Pennsylvania School of Medicine, Philadelphia, delivered the annual N. W. Jones Lectures at the University of Oregon Medical School, Portland, February 9-10. Dr. Landis's topics were "Capillary Pressure, Capillary Permeability and the Movement of Fluid Through the Capillary Wall" and "The Effects of Pressor Drugs and Kidney Extracts on Blood Pressure and Peripheral Blood Flow."

PENNSYLVANIA

Society News.—Drs. Paul Titus and Ralph E. Tafel, Pittsburgh, presented a motion picture on "Human Sterility" at a meeting of the Fayette County Medical Society, Uniontown, March 3.——Dr. Edward L. Bortz, Philadelphia, addressed the Lebanon County Medical Society, Lebanon, March 1, on pneumonia.

Pittsburgh

Society News.—At a meeting of the Pittsburgh Academy of Medicine, February 22, the speakers were Drs. Chester F. Beall, on "Acute Yellow Atrophy of the Liver in the Puerperium"; Robert R. Clark, "Acute Lung Abscess," and Theodore Diller, "Some Problems and Dilemmas."——Dr. Robert W. Staley, among others, addressed the Pittsburgh Neuropsychiatric Society, February 21, on "Insulin Hypoglycemia in Schizophrenia Therapy."

Diabetes Clinic Dedicated.—Dr. Elliott P. Joslin, Boston, was the speaker at the dedication February 8 of an addition to the Children's Hospital to be known as the Renziehausen Memorial Ward and Clinic. The new ward was built with funds provided by Miss Emily Renziehausen, who in August 1937 made available to the hospital a trust fund of a million dollars for research in the causes, treatment and cure of diabetes (THE JOURNAL, Sept. 18, 1937, p. 963). Dr. George Booth is in charge. At the dedication ceremony, held in the auditorium of Mellon Institute, Dr. Joslin announced that he would present to Miss Renziehausen a medal known as the Joslin award in recognition of her twenty years of nursing a brother with diabetes. The Joslin award has previously been given only to Sir Frederick G. Banting, Toronto, one of the discoverers of insulin, and Francis G. Benedict, Ph.D., Boston, who has spent many years in research on diabetes.

UTAH

Annual Registration Due April 1.—All practitioners of medicine and surgery licensed to practice in Utah are required to register annually on or before April 1, with the department of registration, and to pay a fee of $3. If a licentiate fails to reregister within from ninety days to six months after April 1, his license can be revoked and, if revoked, it will be reinstated thereafter only on his paying the delinquent registration fees and an additional year's fee as a penalty.

VIRGINIA

Society News.—Dr. William J. Cusack, Washington, D. C., addressed the Arlington County Medical Society at the Washington Golf and Country Club January 20 on "The Relation of the Endocrines to Menstrual Irregularities."——Dr. Robert DuVal Jones Jr., Norfolk, presented a paper on "Diagnosis of Carcinoma of the Colon" at a meeting of the Northampton County Medical Society January 6.——Dr. Arthur M. Shipley, Baltimore, addressed the Norfolk County Medical Society, Norfolk, January 10, on "The Diaphragm as a Surgical Problem."——Drs. Claude C. Coleman and Carrington Williams, Richmond, addressed the Richmond Academy of Medicine, January 25, on "Neurologic Aspects of Low Back Pain" and

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193

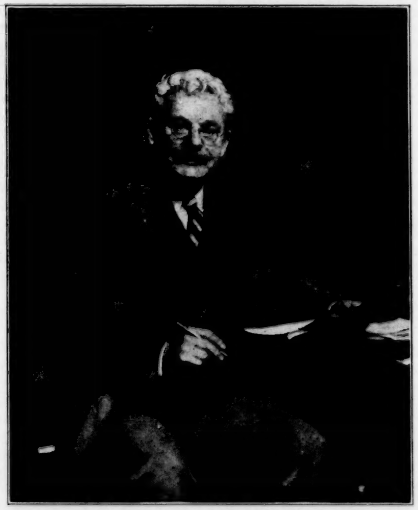
"The Etiology of Malignant Tumors" respectively.——Speakers at a meeting of the Roanoke Academy of Medicine January 3 were Drs. John E. Gardner, on "Electrocardiographic Diagnosis of Cardiac Infarction"; William L. Powell, "Fissure in Ano," and William W. S. Butler Jr. "The Prognosis in Syphilis."

WYOMING

Annual Registration Due April 1.—All practitioners of medicine and surgery licensed to practice in Wyoming are required by law to register on or before April 1, with the secretary of the board of medical examiners, and to pay a fee of $2.50. If a licentiate fails to pay the fee within three months after April 1, his license can be annulled, and if annulled it will be reinstated only on his paying the stated fee, plus $5 as a penalty.

GENERAL

Max Brödel Honored at Saunders Anniversary Dinner.—Mr. Max Brödel, associate professor of art as applied to medicine, Johns Hopkins University School of Medicine, Baltimore, was guest of honor at a dinner in The Barclay, Philadelphia, March 4, given by the W. B. Saunders Company, medical publishers. The occasion marked the firm's fiftieth anniversary. About 200 persons were present. Mr. Lawrence Saunders, president of the company, presented to Johns Hopkins a portrait of Mr. Brödel, a photograph of which is reproduced here. Edward W. Berry, provost of the university, accepted it. Mr. Ryland W. Green, vice president of the Saunders Company, gave the address of welcome. Dr. Thomas S. Cullen, Trustee of the American Medical Association and professor of gynecology at Johns Hopkins, acting as toastmaster, reviewed "The Creation of the Department of Art as Applied to Medicine in the Johns Hopkins Medical School." Dr. Howard A. Kelly, professor emeritus of gynecology, who brought Mr. Brödel to this country in 1894 to illustrate his work, spoke of his contributions to gynecology. Dr. Morris Fishbein, Chicago, Editor of THE JOURNAL, spoke of "Max Brödel's Influence on Medical Illustrating" and Mr. Henry L. Mencken, Baltimore, author and editor, "Max Brödel as a Pianist." Mr. Brödel was born in Leipzig, Germany, June 8, 1870. He received his early education at the Technical High School and the Leipzig Academy of Fine Arts. During vacations he worked in the Anatomical Institute for His, Braune and Spalteholz and in the Physiological Institute for Carl Ludwig and his pupils. In 1890 he was drafted into the army but was required to serve only one year under arms, his second year of military service being devoted to artistic work for his regiment. In 1892 he returned to Leipzig as a free lance artist specializing in anatomic and physiologic illustrations. In 1910 a wish of Mr. Brödel was realized when under an endowment the first School of Art as Applied to Medicine was established at Johns Hopkins and he was placed in charge. Under his direction the school has expanded until it is the largest and most important of its kind in the country. For four years before the school was created, Mr. Brödel was instructor at Johns Hopkins. The portrait of Mr. Brödel is the work of Thomas Corner, Baltimore. Mr. Brödel is an honorary member of the Medical and Chirurgical Faculty of Maryland.



MR. MAX BRÖDEL

Pediatric Board Examinations.—The American Board of Pediatrics announces that it will hold an examination in New York, May 3-4, and in San Francisco, June 12. Dr. Charles A. Aldrich, 723 Elm Street, Winnetka, is secretary of the board.

Central Neuropsychiatric Hospital Meeting.—The annual meeting of the Central Neuropsychiatric Hospital Association will be held in Chicago at the Medinah Club, March 18. Speakers will be Drs. Lloyd H. Ziegler, Wauwatosa, Wis., on "Management and Education of Relatives of Hospitalized Patients"; William C. Menninger, Topeka, Kan., "Modern Treatment of Alcoholism," and Douglas A. Johnston, Cincinnati, "Insulin and Other Shock Treatments in Schizophrenia."

Southeastern Gynecologists and Obstetricians Organize.—The Southeastern Obstetrical and Gynecological Society was organized at a meeting in Charlotte, N. C., February 4, with delegates from North and South Carolina, Virginia, Georgia and Florida. Dr. James R. McCord, Atlanta, was elected president; Dr. Robert E. Seibels, Columbia, S. C., vice president, and Dr. Robert A. Ross, Durham, N. C., secretary. Dr. Marvin Pierce Rucker, Richmond, presided at the organization sessions.

Tri-State Medical Association.—Dr. Jacob F. Highsmith, Fayetteville, N. C., was named president-elect of the Tri-State Medical Association of the Carolinas and Virginia at its meeting in Asheville February 21-22. Vice presidents were elected as follows: Drs. Wright Clarkson, Petersburg, Va.; William L. Pressly, Due West, S. C., and Charles A. Hensley, Asheville, N. C. Dr. James M. Northington, Charlotte, N. C., was reelected secretary. Guest speakers at the meeting included Drs. Henry T. Chickering, New York, on "The Practical Value of Typing in Pneumonia" and Henry J. John, Cleveland, "The Outlook for Diabetic Children." The next meeting will be in Charleston, S. C.

Traffic Safety Awards.—Alfred P. Sloan, chairman of the board of General Motors Corporation, recently gave $25,000 to the Automotive Safety Foundation, which will use the money for additional and personal awards in the national traffic safety contest conducted by the National Safety Council. Twelve police officers and eight traffic engineers will be selected from the prize winning cities and states in the contest to spend a year in study of traffic safety, the former at Northwestern University, Chicago, and the latter at Harvard University, Cambridge, Mass. Each will receive $1,000 in cash, plus a full year's tuition. Results of the contest will be announced early in April.

Changes Recommended in List of Causes of Death.—The committee on the accuracy of certified causes of death, American Public Health Association, announced in *Public Health Reports*, February 4, recommendations for changes in the International List of Causes of Death, which the committee will present at a conference in Paris next October. Among other changes, the committee recommends breaking up Class I in the International List into eight subclasses, as follows: diseases due to bacteria, spirochetes, filtrable viruses, rickettsia, protozoa, helminths, fungi, other infectious and parasitic diseases. It also recommends establishment of subtitles in the group relating to cardiac diseases, to provide for a statistical record of cardiac lesions of rheumatic disease; rearrangement of titles relating to nephritis to bring this group into closer agreement with modern conceptions of the disease; rearrangement of the titles relating to puerperal conditions, designed to meet the needs of the finer analysis of puerperal mortality.

Mortality in Twenty-Seven Cities.—The New York City Department of Health recently published its annual summary of vital statistics of twenty-seven large cities with a total population of more than 27,000,000. The report covers 1936. The crude general death rate for the twenty-seven cities was 11.8, as against 11.4 in 1935. The lowest death rate among them was 8.9 for Milwaukee, followed by 9 for Detroit. The

highest was that of New Orleans, 17.3, with Denver next, 15.7. The report points out that these crude death rates take no account of the age composition of the population, that certain cities have a large proportion of Negroes in their population and that many deaths charged to a city are among nonresidents, a factor influenced by availability of hospital facilities. For the 403,038 births reported by the twenty-seven cities there were 20,055 infant deaths, a rate of 49.8 per thousand live births. The birth rate for the group of cities was 14.8 in 1936 as against 15 in 1935. Chicago and Portland, Ore., had the lowest infant mortality rate among the cities, 39. New Orleans had the highest rate, with 93; Washington, D. C., was next with 72.

Society News.—Dr. George E. Bennett, Baltimore, was chosen president-elect of the American Academy of Orthopedic Surgeons at its annual meeting in Los Angeles in January. Dr. John C. Wilson, Los Angeles, was installed as president. Dr. Clarence B. Francisco, Kansas City, Mo., was elected vice president, and Dr. Carl E. Badgley, Ann Arbor, secretary. Dr. Philip Lewin, Chicago, received the principal award, a gold medal, for the best exhibit; his subject was teaching orthopedics to undergraduate students. The 1939 convention will be held in Memphis, Tenn.——Dr. Harold L. D. Kirkham, Houston, Texas, was elected president of the American Association of Oral and Plastic Surgeons at its annual meeting in Houston and Dallas, January 31 and February 1. Dr. Gordon B. New, Rochester, Minn., was elected vice president and Dr. Ernest Fulton Risdon, Toronto, secretary. Dr. James T. Mills was host to the meeting at Baylor Hospital in Dallas and Dr. Kirkham at Jefferson Davis Hospital in Houston. Membership in the association is limited to fifty.——Dr. Roy B. Harrison, New Orleans, was chosen president-elect of the Federation of State Medical Boards of the United States at the annual meeting in Chicago February 15. Dr. Henry J. Lehnhoff, Lincoln, Neb., is president and Dr. Julian F. Du Bois, Sauk Centre, Minn., vice president. Dr. Walter L. Bierring, Des Moines, Iowa, was reelected secretary.

CANADA

Personal.—Dr. Edward W. Archibald, formerly head of the department of surgery, McGill University Faculty of Medicine, Montreal, received the honorary degree of doctor of medicine from the University of Paris at a ceremony at McGill January 11. Count Robert de Dampierre, minister of France to Canada, made the presentation.

LATIN AMERICA

New Health Officials in Mexico.—Dr. Leonidas Almazán, former minister from Mexico to Germany, has been appointed director of public health of Mexico, it is reported. He succeeds Dr. José Siurob, who is now director of health for the federal district, including the city of Mexico. It is also reported that Dr. Enrique Hernández Alvarez has been made secretary of public welfare.

Tuberculosis Campaign in Cuba.—The Cuban government has recently allotted $1,000,000 from its lottery funds for a campaign against tuberculosis, the *Health Officer* reports. Clinics are to be established throughout the country for examinations, which will be carried out on every citizen. Dr. Edgar Mayer and Morton C. Kahn, Ph.D., New York, recently visited the island to help establish the first clinics. With Dr. Wilson G. Smillie, New York, they will return periodically to advise in the work, it is said. L'Esperanza Hospital near Havana has been renovated for the care of tuberculous patients and a new hospital is being built near Trinidad.

FOREIGN

Society News.—The seventh International Congress of Genetics will meet in Edinburgh in 1939, probably August 23-30, according to *Science*. Prof. Francis A. E. Crew of the Institute of Animal Genetics, University of Edinburgh, has been appointed general secretary.——The German Society for Circulatory Research will hold a meeting March 26-27 in Bad Nauheim. The subject of discussion will be "Circulatory Collapse."

International Congress for History of Medicine.—Applications to attend the ninth International Congress for the History of Medicine in Yugoslavia September 3-11 should be made to Dr. Vladimir Bazala, secretary general of the congress, 95 Vlaska ulica, Zagreb, Yugoslavia. The congress will open in Zagreb and other meetings will be held in Belgrade, Sarajevo and Dubrovnik. Applications to address the congress should be made as soon as possible by cablegram, naming the subject to be treated, according to an announcement.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Feb. 12, 1938.

Radiotherapy in Nonmalignant Gynecologic Conditions

At a joint meeting of the Sections of Radiology and of Obstetrics and Gynecology of the Royal Society of Medicine a discussion took place on radiotherapy in nonmalignant gynecologic disorders. It was opened by Dr. W. M. Levitt, radiologist, who said that the time had come to formulate indications for radiotherapy in fibromyoma. X-rays had given good results for over thirty years; the bleeding stopped and the fibroid diminished and sometimes even disappeared. The mode of action was mainly through the ovaries. Consistently good results postulated sterilization, which was equally effective without direct irradiation of the fibroid. In patients under 40, radiotherapy was excluded unless the condition was so extensive as to make successful pregnancy impossible. The contraindications applied only to a small minority of cases—very large fibroids causing pressure symptoms, acute complications and degeneration in the fibroid. High voltage x-rays were now always used and were given in six daily applications.

Another indication for radiotherapy was endometriosis. The radiologist had to consider whether he would destroy the tumor by direct irradiation or whether sterilization also was necessary. Interstitial radium might give better results than x-rays, and sterilization might be avoided in certain cases, especially when the disease was situated in the rectovaginal septum. Radiotherapy was also the method of choice for irregular function and hemorrhage at or near the menopause, but in younger patients it had the same limitations as for fibroids. Only in grave cases, such as severe hemorrhage at puberty, should this rule be relaxed.

Dr. J. F. Bromley, radiologist, discussed extra-uterine conditions. Radiotherapy gave good results in many cases of acromegaly, especially in relieving the unbearable headache. Hypertrophy of the parathyroid causing bony atrophy could sometimes be relieved. Menorrhagia was often caused by hypersecretion of estrogen, and direct irradiation would sometimes arrest the function of the ovaries.

Mr. L. Phillips, gynecologist, said that in menopausal menorrhagia castration doses of radiotherapy gave better results in every way than surgery. There was less hospitalization, and the mortality and morbidity were lower. Radium produced disturbances of metabolism, peritonitis and uremia, but the death rate was under 1 per cent, a low figure compared to hysterectomy. A castration dose of x-rays would induce the menopause over a longer period and more gradually than radium. It was suitable for large tumors and not contraindicated by pelvic inflammation.

Prof. Miles Phillips, president of the Section of Obstetrics and Gynecology, referred to the stimulating effect of x-rays. A woman of 29, who had not menstruated for ten years, began to do so after roentgen therapy and gave birth to two boys. He suggested that the dose might have destroyed a corpus luteum which was preventing ovulation. The bulk of evidence suggested that radium acted on the ovary. If it was inserted in the second half of the cycle the patient would probably have another period; if inserted in the first half she probably would not.

Torsion of the Hydatid of Morgagni

Torsion of the testicle or axial rotation of the spermatic cord has long been recognized, but torsion of the little appendix termed "the hydatid of Morgagni" has been known only since 1922. Though it seems to be commoner than has been supposed, it has seldom been recognized and is generally mistaken for spontaneous epididymo-orchitis at or about puberty. Though

the first cases were recorded by English writers (Colt, Shattock and Walton), it is largely to French writers, especially Mouchet, that credit is due for establishing the clinical syndrome. In the *British Journal of Surgery* Dr. John Lambert of Wellington College and Dr. R. E. Smith of Rugby have reported nine cases of torsion of the testicle and of the hydatid of Morgagni. As three of these cases belong to the latter category, their proportion bears out the view that the condition is not so uncommon as might be supposed. The general signs differed little from those seen in torsion of the spermatic cord; therefore the diagnosis must depend on accurate interpretation of local signs. The first patient, a youth of 17, had a sudden attack of pain in the left testicle at about 5 a. m. There was some swelling and marked tenderness of the upper part of the epididymis. The spermatic cord was not swollen or tender. In the evening the temperature rose to 100 F. Next day the testicle and epididymis were greatly swollen. He had a slight evening elevation of temperature and a surgeon suggested acute tuberculosis of the testicle. There was a gland scar in the neck. He was sent home and sixteen days after the onset came under the care of Sir John Fraser of Edinburgh, who operated and found torsion of the cord and the testicle in a condition of complete necrosis. Examination of the specimen showed that the torsion began in the hydatid of Morgagni, which had an unusually long pedicle.

PARIS

(From Our Regular Correspondent)

Feb. 12, 1938.

Periodic Medical Examination of Automobile Drivers

At the January 25 meeting of the Académie de médecine a paper was read by Professor Parisot and Dr. G. Richard of Nancy on medical examination of automobile drivers. In 1937 there were 1,700,000 passenger automobiles and 155,000 trucks here as compared with 100,000 twenty years ago. During the last few years there have been between 3,000 and 4,000 deaths and from 50,000 to 70,000 injured annually in France, despite numerous precautions taken to prevent automobile accidents. At the sixteenth medicolegal congress, held in 1931, it was shown that more deaths were due to automobile injuries than to typhoid and diphtheria combined. The human factor is responsible for accidents in from 36 to 80 per cent, according to various statistics cited. Medical examination of chauffeurs has been advocated by the Académie de médecine since 1930. Such tests are already obligatory for drivers of passenger cars and trucks in seventeen European countries. In four others (France, Austria, Belgium and Switzerland) such an examination is required only of truck drivers. Gratifying results have been noted in Paris since 1928, when medical examination was first required, of all candidates for positions as chauffeurs and mechanics of motor busses and subway trains in Paris. In 1923 there was one accident for each 105,000 passengers and in 1936 only one to 212,300 passengers.

The authorities here have always opposed extension of obligatory medical examination to all chauffeurs, citing England as an example of a country in which there are comparatively few accidents although medical examination is not compulsory. The authors showed the fallacy of this argument by citing statistics of automobile accidents in both England and the United States. There were 204,710 accidents in England in 1933, and as the result of more strict control of the granting of driving licenses this number dropped to 195,892 in 1935. There were 7,343 deaths in 1934 as compared to 6,502 in 1935, and the number of injured dropped from 231,603 in 1934 to 221,726 in 1935. A system of periodic examinations for all taxicab drivers who were above a certain age or showed physical defects was instituted in England in 1936. Every chauffeur above the age of 50 is obliged to submit to a medical examination every six years up to the age of 65, every five years between the ages of 65 and 73, and every year thereafter.

A number of examples were mentioned by the authors of fatal accidents due to cardiovascular disturbances in chauffeurs. The authors advocated the passage of a law in France making periodic medical examinations obligatory. This should be carried out according to the following schedule: every six years for all chauffeurs from 18 to 45 years of age, every five years between the ages of 45 and 55, every three years between the ages of 55 and 60, every two years between the ages of 60 and 65 and every year above the age of 65.

Following the reading of this paper, a committee of six fellows of the Académie de médecine was appointed to draw up a law covering these recommendations.

BCG Tuberculosis Vaccine in Children

At the February 1 meeting of the Académie de médecine a paper by Dr. A. de Carvalho of Rio de Janeiro, Brazil, was read by Dr. Guérin of the Pasteur Institute of Paris. Thirty-eight families in which tuberculosis existed were observed by Dr. Carvalho over a period of eight years. Of 101 children constantly exposed to infection from tuberculous parents, forty-eight were given the BCG vaccine by mouth from the time of birth and the remaining fifty-three were not vaccinated. In twenty-five of the families there were only two children, one of whom was vaccinated and the other not. Neither the vaccinated nor the nonvaccinated children were isolated. The result was a tuberculosis morbidity of 20.8 per cent among the vaccinated and of 39.6 per cent among the nonvaccinated children and a mortality from tuberculosis among the vaccinated children of 2.1 per cent as compared to one of 13.2 per cent among the nonvaccinated. Two thirds of the deaths in the unvaccinated group occurred during the first twelve months after birth.

Tuberculin Epidermal Reactions in Pupil Nurses

At the January 11 meeting of the Académie de médecine a paper was read by Professor Rist and his associates in which the results of a study of tuberculin epidermal reactions in 165 pupil nurses of one of the large training schools were reported. All of the pupil nurses had x-ray examination of the lungs; the family and previous histories did not reveal the presence of tuberculosis. During 1935, 165 probationers were admitted to the schools, of whom 144 were given ward service as a part of their course and the remainder were to be trained for administrative work. The latter group was not exposed to tuberculous infection in the wards, as were those in the first group. The epidermal tuberculin tests on admission to the training school were positive in about the same proportion in the two groups, 58.33 and 61.90 per cent. Tuberculin epidermal tests were made in June 1936 and January 1937 and were repeated in October 1937. At the last named date, two years after admission to the training school, forty-six of sixty-eight pupil nurses who had entered with a negative epidermal tuberculin test had a positive reaction. In other words, a primary infection had taken place during the first two years of their training period. The percentage of positive reactions was much higher, 88.73, in the first group, who had been exposed to infection in the wards, than in the second group, who had not been so exposed. The test remained negative in sixteen of the sixty pupil nurses whose reaction had been negative on admission to the school. In six of the forty-four pupil nurses whose negative test on admission had changed to a positive one during the two years school term, both clinical and roentgenologic signs of a more or less severe pulmonary tuberculosis appeared. One of these six pupil nurses died from such an infection. Professor Rist and his associates were of the opinion that their results confirmed the observations of Heimbeck at the nurses' training school in Ulleval, who found that both the relatively high morbidity and mortality from tuberculosis had been greatly reduced as the result of the use of the BCG vaccine on admission to the school. The authors believed that it might be advisable to study the question of employing such vaccination in pupil nurses in France.

Auto-Agglutination of Red Blood Cells

An unusual case of agglutination of a patient's red blood cells by his own serum was reported at the Dec. 17, 1937, meeting of the Société médicale des hôpitaux of Paris by Dr. P. Michon and his associates. This condition is rare, all the reported cases up to 1930 having been cited in an article by one of the authors. Since that time, four other cases have been reported. In the case reported by Michon and his associates, a young chemist had been treated for asthenia in 1932. There had been, at that time, a marked alkalosis (7.58) and a mononucleosis of 42 per cent. Following inhalation of large amounts of gasoline vapor in April 1937, symptoms of pulmonary congestion appeared. The first enumeration of the red blood cells was attempted about four weeks later but was found to be impossible because of an auto-agglutination. A drop of blood left at room temperature, after having been diluted with two drops of physiologic solution of sodium chloride to slow up the agglutination, showed a fusiform elongation of the red blood cells and the production of lines of force. The last two changes are termed the Sandow phenomenon, as described by Zimmer in 1936, and are considered typical of iso-agglutination. The patient's serum agglutinated human red blood cells of all four groups. Although the bleeding time was only three minutes, the coagulation time was twenty-one minutes. The clinical symptoms during the following three months indicated a vasomotor dysfunction. By July 21 the auto-agglutination had entirely disappeared, both the red blood cells and serum showing reactions typical of group 2; the coagulation time was still prolonged, twelve minutes, but no evidence of hemophilia appeared at any time. The authors were of the opinion that the cause of the temporary phenomenon of auto-agglutination was the inhalation of large quantities of gasoline vapor.

Death of Professor Doleris

Professor Doleris, one of the most prominent French gynecologists and obstetricians of the nineteenth century, died Jan. 22, 1938, aged 86. His graduating thesis, published in 1882, on the bacteria found in puerperal fever, represented work done under the supervision of Pasteur. Aside from the streptococcus and staphylococcus as causative organisms, he called attention to the important part played by certain other organisms, especially the gangrene producing bacteria. Doleris was gynecologist and obstetrician at one of the large Paris hospitals for many years. He was one of the first to advocate round ligament suspension of the retroverted uterus.

BERLIN

(From Our Regular Correspondent)

Jan. 17, 1938.

Medicolegal Decisions Relative to the Value of Nature Medicine

The recent report on Nature Medicine and the heilpraktiker must needs be supplemented by further medicolegal news items. Of special interest were the criminal proceedings brought against not a heilpraktiker (lay practitioner) but a licensed physician who was charged with criminal negligence. He had refrained from the administration of diphtheria antitoxin in a correctly diagnosed case. The defendant, a practitioner of Nature Medicine, was still treating the patient, a girl aged 17, with swabbings and poultices as late as the fourth day of illness and after the diagnosis of diphtheria had been established. Only on the sixth day did he authorize transfer of the patient to a hospital, where she died. The public prosecutor asked a ten months jail sentence but the doctor was acquitted. The phrasing of the court's decision in this case offers an interesting sidelight on current medicolegal ideology. Much weight was given the contention that the defendant had tried several procedures considered rational according to the standards of Nature Medicine but that, owing to the rapid advance of the infection, these had been ineffectual. Against the defendant was his failure to acquaint the girl's parents with the importance of inoculation, a measure generally regarded as infinitely more effective than any procedure of Nature Medicine. But there is no law under which a practitioner can be held responsible for the fatal termination of a case simply on the basis of his abstention from utilizing a procedure, even one which in all probability would preserve the patient's life. In the case under discussion the two expert medical witnesses, a professor of internal medicine and a professor of pediatrics, stated that the experimental limits for the favorable effect of diphtheria antitoxin lay between 70 and 75 per cent, a figure which in any event would refute the allegation of criminal negligence.

Another case of alleged criminal neglect in the treatment of diphtheria was reviewed by the supreme court of Germany. The defendant, a physician of Frankfort-on-the-Main, was charged with criminal responsibility in the deaths of three diphtheria patients whom he had treated according to homeopathic methods. Regular medical measures such as administration of antitoxin had been omitted. The court of first instance acquitted this man. The public prosecutor then asked the supreme court to set aside the judgment of the lower court. The highest tribunal, in denying the prosecutor's appeal, expressed the following opinion: The relative superiority of "allopathic" methods as opposed to homeopathic methods or vice versa has thus far not been sufficiently proved either in theory or in practice; accordingly a rejection of the principle of serotherapy by the defendant cannot be construed as a criminal offense. Moreover, evidence had been adduced to show that the practitioner had successfully treated a majority of his diphtheria patients by homeopathic methods. Therefore, held the court, he was under no obligation to administer antitoxin in the cases under discussion.

The foregoing examples illustrate the trend of juridical opinion in present-day Germany with regard to the serotherapy of diphtheria.

On the other hand, several heilpraktiker have recently been convicted of criminal negligence in connection with the deaths of patients (The Journal, January 8, p. 141). One case concerned the death of a child from acute appendicitis and peritonitis. The defendant, who had passed the official examination required of heilpraktiker and was a prominent member of the heilpraktiker's league, had diagnosed the illness as "gastroenteric catarrh" and prescribed various homeopathic medications for its relief. A regular physician was called in but too late. According to the expert testimony heard at the trial the child's life could have been saved if adequate medical management had supervened in time. The defendant was found guilty and sentenced to one year in jail and suspension of his license for three years. It is noteworthy that the court ordered the heilpraktiker into custody immediately following the conviction; apparently it was suspected that the man contemplated flight.

In another case a heilpraktiker was convicted of manslaughter in a Berlin court and sentenced to six months' imprisonment. This man had as patient a woman affected with cancer of the breast, whom he treated with homeopathic medications over a long period. He had also advised the woman against visiting a doctor. When the patient finally came to surgical intervention the malignant condition was far advanced and she died. It is characteristic that in deciding on a relatively light punishment the court took into consideration that the convicted man had not previously been a defendant in any criminal proceeding.

An illuminating article on the problems of irregular medicine entitled "Improper Expert Testimony in Criminal Proceedings Against Quackery" has just appeared in the official *Deutsches Aerzteblatt*. The author is Dr. A. Hellwig, an eminent jurist who for many years has made a special study of medicolegal problems and of quackery in general. He points

out that convictions of quacks for fraud and for criminal negligence with fatal result to the patient are extremely difficult to obtain even when the guilt of the accused seems undoubted. This failure to convict is often due to introduction of unsatisfactory expert testimony by the prosecution as well as to the arbitrary and involved questions raised by expert testimony in general. As every one knows, even the most nonsensical alleged curative methods will not lack enthusiastic adherents. In a number of quackery trials, experts in the occult have been called on to defend the efficacy of occult therapeutics and these witnesses may even be licensed physicians. Then too the prosecution may call in as expert witnesses medical officials and other doctors who are inadequately prepared and unequal to the task; this deficiency on the part of the prosecution's witnesses often leads to a failure to convict even in proper cases.

In a case in point, a magnetic healer treated by telephone a child who ultimately succumbed to diphtheria. Placed on his trial for criminal negligence, the man was acquitted. The main thesis of his defense was that the absent treatment had actually increased the sick child's vitality and even effected temporary improvement in the general condition. The expert testimony of the local medical official was garbled in the extreme and this circumstance doubtless contributed to the outcome. Moreover, another medical witness (whose license has since been revoked) stated under oath that telephonic transmission of vital magnetism is in fact an effective therapeutic procedure even in diphtheria.

From the foregoing and other instances, Dr. Hellwig concludes that official medical experts and other doctors who are called on to testify in quackery trials ought to come into court better prepared. Above all, these experts should be in a position to express clear and unequivocal opinions which indicate that the problems involved have been considered from the standpoint of medical science.

News of the Profession

It has just been announced that the doctors of the Berlin Sick Insurance are to be guaranteed a minimal income by the official medical organization. Legitimate panel practitioners are hereafter assured of a total annual income of 1,000 marks. A doctor whose annual income falls below that amount may be granted the difference between his actual income and 1,000 marks. The practitioner himself must make application for this assistance; he will be required to furnish precise data concerning his total professional income and his private assets. The necessary funds for this aid are contributed by the more prosperous panel physicians. This is made feasible by the fact that the remittance of panel practitioners' honorariums is carried on by the Medical Organization. This New Year's present is intended to benefit only the so-called German-blooded doctors.

New restrictions have been placed on Jewish doctors; since the first of January they have been barred from practice in the so-called Supplementary Clubs. The men affected were apprised of their exclusion only at the moment it became a fact. The membership of the Supplementary Clubs comprises chiefly clerical and industrial workers, who are less likely to be incapacitated than members of the Municipal Clubs, for example. Accordingly, panel practitioners in the Supplementary Clubs have been assured of a slightly better income. Even Jewish doctors who saw active service or who lost sons in the World War were not exempted from this expulsion. Jewish doctors have also been excluded from the welfare practice as well as from panel practice among the insurance clubs of postal employees and policemen, the big employees' organizations of the Berlin Transportation Company and the Siemen Telegraph Company and in addition the insurance of the National Student Association and so on (some of these clubs had previously introduced similar restrictive measures). The new restrictions affect some 3,000 Jewish practitioners, about 800 of whom are in Berlin. Much publicity had been given the circumstance that one third of the panel practitioners were still Jews and this led directly to enactment of the new restrictions.

Favorable Expansion of the Sickness Insurance

Provisional 1937 statistics for the aggregate of official Sick Insurance organizations indicate an excess of income over expenditure. The number of clubs declined somewhat during the year; there are now 4,598 such units. Total membership increased from 19,400,000 to 22,900,000. Official circles are now attempting to place all Sick Insurance more within the scope of national-political economics. For example, insurance club members with large families are to be eligible for more substantial benefits without any additional contributions being required of them.

Just released by the National Bureau of Statistics are some figures on Sickness Insurance disbursements during the year 1935. These statistics, shown in the accompanying table, represent in round numbers the amounts paid out for various purposes by the clubs under direct governmental control, by the Miners' Clubs and by the Supplementary Clubs.

Sickness Insurance Disbursements During 1935

Medical and dental treatment	461,000,000 marks
Therapeutic substances and appliances, hospital care and convalescent care	324,000,000 marks
Care of members' dependents	97,000,000 marks
Care during confinement	110,000,000 marks
Prophylaxis and hygiene	5,500,000 marks

Thus exclusive of the cash benefits paid to members and the costs of administration around 998,000,000 marks was expended by the Sickness Insurance in 1935. It is estimated that the expenditures during 1936 were about 4 per cent greater than in 1935.

JAPAN

(From Our Regular Correspondent)

Jan. 27, 1938.

Prevention of Venereal Disease in Tokyo

The Metropolitan Police Board reports as follows on the preventive measures it applies continually to the licensed and unlicensed prostitutes and to the geisha girls: The licensed prostitutes who are confined in restricted quarters are examined once a week, and any with venereal disease must enter a hospital attached to this office. The brothels are inspected every month by the police, and a member of the sanitary committee goes round for inspection. He spares no efforts to aid the keepers in how to improve their equipment. Occasionally a lecture on the prevention of this disease is given by an expert to the prostitutes. Generally speaking, any order given by the police is obeyed. There has been a remarkable decrease of infection in these quarters. The "geisha girls," who are singers and dancers, are sometimes little better than the prostitutes; they also are advised, though not compelled, by the police to have a regular examination at their own will or by the agreement of their unions, which number seventy in all in Tokyo; sixty-eight unions have their own doctors, but still the result is not good enough. Two venereal disease prevention parties were recently formed by the metropolitan police board, whose duty it is to teach health to those women. The society for the prevention of venereal disease has a group that goes round the city to exhibit moving pictures, which give citizens an insight into the prevention of venereal disease.

Preservation of Vaccine Lymph

In November at the Infectious Disease Research Institute in Tokyo a paper was read by Dr. Yaoi on the preservation of vaccine lymph. He is mentioned as a probable candidate for the prize of the Imperial Academy for 1937. He said: "The

purified vaccine matter as well as the common matter can hardly remain effective over half a month in summer temperature. As for the vessel in which to keep the lymph, the brown one used widely, which is colored with iron, is very harmful, but the brown ampule made of carbon is innocuous. Concerning temperature, the lymph can remain effective for a week in summer when the temperature is 86 F., which temperature is the highest one on an average in Tokyo and its vicinity. It is effective for a month when the temperature varies between 63 and 68."

New Welfare Department

The present cabinet announced last July the establishment of the department for the promotion of the public welfare. Originally the establishment of this office was proposed by the war office and it was at first to be called the health office. The appearance of this office is an epoch-making change, for it aims to bring all government administration of sanitation under a single authority. At its opening, January 11, Prince Konoe, the prime minister, said he was greatly pleased to have an office to unify the affairs of national health, labor and social reform. The office aims to strengthen and extend the former administrations, and the chief aim should be to raise the level of the nation's health. Marquis Kido, minister of education, was appointed to be minister of welfare as an additional office for the time being. The new office has five bureaus of physical training, sanitation, social welfare and labor, and an independent bureau of life insurance is attached to it. It was established at an estimated cost of $25,000,000 for the coming fiscal year.

Prevention of Mental Diseases

The Association of the Mental Homes of Japan held its sixth general meeting in November and passed a resolution to be presented to the minister of home affairs to recommend methods for prevention of mental disease. Almost at the same time the Japan society of mental diseases made a similar proposal to the government as an urgent necessity, judging from the present state of society. Prevention, first of all, requires more hospitals, for at present only 6 per cent of the cases can be accommodated. As the causes of mental diseases are to be the subject of research, there must be established on a large scale a mental disease research institute by the government. An office where parents can consult the alienist about their children should be founded by the government at as many places as possible throughout the country.

Marriages

SNOWDEN C. HALL JR., Danville, Va., to Miss Ida Shankle Hardman of Commerce, Ga., in December 1937

EDWARD CARLISLE JOYNER, Suffolk, Va., to Miss Ruth Elizabeth German of Richmond, Dec. 6, 1937.

KENNETH E. STEIN, Lakeville, Minn., to Miss Mary Phyllis Baudin of Minneapolis, Aug. 24, 1937.

HERBERT SHERWIN, Fall River, Mass., to Miss Delle Silverman of Cambridge in August 1937.

ALBERT ALLEN to Miss Mildred Soncrant, both of San Pedro, Calif., in Yuma, Ariz., January 1.

HENRY A. BELLAFSKY, Woodbridge, N. J., to Miss Rose Buckner of Newark, January 2.

ALBERT E. LONG, Charlottesville, Va., to Miss Lois Nichols at Lynchburg, Dec. 27, 1937.

HAROLD W. SHUTTER to Mrs. Gazelle Christman, both of Milwaukee, Nov. 23, 1937.

PAUL SADLER KEMP, Macon, Ga., to Miss Mildred Burnley of Augusta, January 6.

JULIUS ROOS, Chicago, to Miss Gretel Marx of Flonheim, Germany, recently.

Deaths

James Lancelot Minor, Cordova, Tenn.; University of Virginia Department of Medicine, Charlottesville, 1876; member of the Tennessee State Medical Association; emeritus professor of ophthalmology, University of Tennessee College of Medicine, Memphis; member of the American Ophthalmological Society; fellow of the American College of Surgeons; served during the World War; formerly on the staffs of the Memphis Eye, Ear, Nose and Throat Hospital, St. Joseph's Hospital, Baptist Hospital and the Memphis General Hospital; aged 83; died, Dec. 3, 1937.

William Charles McLaughlin, Providence, R. I.; Harvard University Medical School, Boston, 1905; member of the Rhode Island Medical Society, New England Ophthalmological Society and the New England Otological and Laryngological Society; fellow of the American College of Surgeons; on the staffs of the Charles V. Chapin Hospital, Providence City Hospital, Rhode Island Hospital and St. Joseph's Hospital; aged 57; died, Dec. 6, 1937, of duodenal ulcer and dilatation of the heart.

George Hoskins Scott ✠ Colonel, M. C., U. S. Army, Fort Slocum, N. Y.; University of Pennsylvania Department of Medicine, Philadelphia, 1902; member of the House of Delegates of the American Medical Association in 1933; entered the army as an assistant surgeon in 1902; was promoted through the various grades to that of colonel in 1928; fellow of the American College of Surgeons; aged 58; was found dead, Dec. 13, 1937, in Detroit, of carbon monoxide poisoning.

Walter Herbert Blakeslee ✠ Philadelphia; Johns Hopkins University School of Medicine, Baltimore, 1901; at one time physician to the State Department of Labor and Industry and the Workmen's Compensation Board; formerly on the staff of the Episcopal Hospital; aged 66; died, Dec. 13, 1937, in the Temple University Hospital, of left inguinal hernia and thrombosis.

Charles Ulysses Moore ✠ Portland, Ore.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1910; fellow of the American College of Physicians; served during the World War; on the staff of the Multnomah Hospital; author of "Nutrition of Mother and Child"; aged 60; was found dead, Dec. 21, 1937, of accidental carbon monoxide poisoning.

Dan Smith Renner ✠ Skillman, N. J.; University of Louisville (Ky.) Medical Department, 1909; past president of the Somerset County Medical Society; member of Medical Society of New Jersey and the American Psychiatric Association; superintendent of the New Jersey State Village for Epileptics; aged 53; died, Dec. 13, 1937, of coronary thrombosis.

William Worthington Samuell ✠ Dallas, Texas; Tulane University of Louisiana Medical Department, New Orleans, 1901; fellow of the American College of Surgeons; served during the World War; on the staffs of the Baylor University, Dallas Methodist and St. Paul's hospitals; aged 59; died, Dec. 12, 1937, in a local hospital, of coronary occlusion.

H. Christian U. Midelfart ✠ Eau Claire, Wis.; Kongelige Frederiks Universitet Medisinske Fakultet, Oslo, Norway, 1892; fellow of the American College of Surgeons; on the staffs of the Lutheran and Sacred Heart hospitals; aged 72; died, Dec. 14, 1937, of coronary sclerosis, chronic myocarditis, mitral insufficiency and bilateral cystic kidneys.

Frank Harold McLaury ✠ New York; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1895; served during the World War; medical director of the Chase National Bank; aged 64; died, Dec. 8, 1937, in the New York Post-Graduate Medical School and Hospital, of coronary thrombosis.

William Griggs Marsh, Watsontown, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1877; member of the Medical Society of the State of Pennsylvania; for many years member of the school board and board of health; aged 85; died, Dec. 29, 1937, of chronic endocarditis, nephritis and arteriosclerosis.

George Malcolm Graham ✠ Austin, Texas; University of Texas School of Medicine, Galveston, 1912; for many years director of laboratories for the state department of health; served as pathologist to the Seton Infirmary and St. David's Hospital; aged 51; died, Dec. 25, 1937, in a local hospital, of encephalitis.

Martin Joseph Patrick, Shenandoah, Pa.; Temple University School of Medicine, Philadelphia, 1910; member of the Medical Society of the State of Pennsylvania; for many years

member of the local board of health; on the staff of the Locust Mountain Hospital; aged 52; died, Dec. 9, 1937, of coronary thrombosis.

Felix Summerfield Martin, Beaumont, Texas; Barnes Medical College, St. Louis, 1894; past president of the Jefferson County Medical Society; formerly connected with the Indian Service; aged 67; died, Dec. 23, 1937, in a local hospital, of coronary thrombosis, diabetes mellitus and arteriosclerosis.

Arthur Levan Page ✠ Harrisburg, Pa.; Jefferson Medical College of Philadelphia, 1907; member of the American Academy of Pediatrics; aged 54; on the staffs of the State Hospital for Crippled Children, Elizabethtown, and the Harrisburg Hospital, where he died, Dec. 22, 1937, of arteriosclerosis and nephritis.

Ford Eastman ✠ Erie, Pa.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1908; fellow of the American College of Surgeons; past president of the Erie County Medical Society; on the staff of the Hamot Hospital; aged 59; died suddenly, Dec. 28, 1937, of cerebral hemorrhage.

Walter James Miller, Johnson City, Tenn.; Vanderbilt University School of Medicine, Nashville, 1877; member of the House of Delegates of the American Medical Association in 1903, 1905, 1906; past president of the state board of health; aged 82; died, Dec. 14, 1937, of carcinoma of the larynx.

John H. Dripps, Philadelphia; Jefferson Medical College of Philadelphia, 1878; member of the Medical Society of the State of Pennsylvania; for many years on the staff of the Stetson Hospital; aged 80; died, Dec. 20, 1937, of arteriosclerosis, pyelonephritis and coronary embolism.

Harvey Leander Kennedy, Ottawa, Kan.; Kansas Medical College, Medical Department of Washburn College, Topeka, 1903; member of the Kansas Medical Society; past president and secretary of the Franklin County Medical Society; aged 68; died, Dec. 28, 1937, of coronary disease.

Oscar Benjamin Millard, Harrisburg, Pa.; Jefferson Medical College of Philadelphia, 1928; member of the Medical Society of the State of Pennsylvania; on the staff of the Harrisburg Polyclinic; aged 36; died, Dec. 29, 1937, of injuries received when struck by an automobile.

William Armitage Moncrieff ✠ New Bedford, Mass.; Tufts College Medical School, Boston, 1913; member of the New England Otological and Laryngological Society; served during the World War; aged 47; died, Dec. 18, 1937, of tuberculosis of the lungs and larynx.

Homer Hill Lewis ✠ Clearfield, Pa.; University of Louisville (Ky.) Medical Department, 1909; served during the Spanish American and World wars; formerly county coroner; aged 59; on the staff of the Clearfield Hospital, where he died, Dec. 18, 1937, of coronary occlusion.

William Beach Morrow, Walton, N. Y.; Bellevue Hospital Medical College, New York, 1881; member of the Medical Society of the State of New York; past president of the board of education; aged 79; died, Dec. 18, 1937, of cerebral hemorrhage and chronic nephritis.

William Scott Piper ✠ Clearfield, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1904; served during the World War; fellow of the American College of Surgeons; on the staff of the Clearfield Hospital; aged 55; died, Dec. 15, 1937, of coronary occlusion.

James Melvin Little, Sterling, Kan.; Western Reserve University Medical Department, Cleveland, 1898; member of the Kansas Medical Society; formerly mayor of Sterling; president of the county board of health; aged 65; died, Dec. 27, 1937, of heart disease.

Joseph B. Champion, Montoursville, Pa.; Medical College of Indiana, Indianapolis, 1898; veteran of the Spanish-American War; at one time a lawyer; aged 70; died, Dec. 13, 1937, in the Danville (Pa.) State Hospital, of cerebral arteriosclerosis and coronary occlusion.

John Emerson Hunter, Greenville, Ohio; Cincinnati College of Medicine and Surgery, 1891; member of the Ohio State Medical Association and the Associated Anesthetists of the United States and Canada; aged 76; died, Dec. 29, 1937, in Alexandria, La.

Emanuel Norman Martin ✠ Clay Center, Kan.; University Medical College of Kansas City, Mo., 1900; past president and secretary of the Clay County Medical Society; county health officer; aged 63; died, Dec. 16, 1937, in Halstead, of carcinoma.

Arthur Daniel Morgan, North, S. C.; Medical College of the State of South Carolina, Charleston, 1890; served during the World War; aged 71; died, Dec. 31, 1937, in the Veterans Administration Facility, Columbia, of lobar pneumonia and arteriosclerosis.

Louis Edwin Jones ✠ Prescott, Wis.; University of Minnesota Medical School, Minneapolis, 1924; medical director and owner of St. Croixdale Sanatorium; aged 40; died, Dec. 28, 1937, of cerebral hemorrhage, coronary occlusion and arteriosclerosis.

Herman David Jerowitz ✠ Kansas City, Mo.; University Medical College of Kansas City, Mo., 1891; an Affiliate Fellow of the American Medical Association; on the staff of the Menorah Hospital; aged 68; died, Dec. 24, 1937, of heart disease.

George Watson Barnett, Johnstown, Pa.; Jefferson Medical College of Philadelphia, 1908; fellow of the American College of Surgeons; veteran of the Spanish-American War; aged 60; died, Dec. 17, 1937, of pulmonary embolus and heart disease.

Robert Allen McCurdy, Eldorado, Kan.; University of Kansas School of Medicine, Kansas City, 1933; member of the Kansas Medical Society; aged 29; died, Dec. 15, 1937, in the Temple University Hospital, Philadelphia, of carcinoma.

David Gillison Wells, McHenry, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1898; aged 68; died, Nov. 26, 1937, in Los Angeles, of gastric hemorrhage and acute dilatation of the heart.

Walter August Day, Alton, Ill.; Bennett Medical College, Chicago, 1914; served during the World War; aged 47; on the staff of St. Joseph's Hospital, where he died, Dec. 30, 1937, of hypostatic pneumonia and cardiorenal vascular disease.

Edwynn J. Oxford, Chambers, Neb.; John A. Creighton Medical College, Omaha, 1905; member of the Nebraska State Medical Association; aged 55; died, Dec. 7, 1937, in St. Joseph's Hospital, Omaha, of arteriosclerosis and heart disease.

Charles La Forge Manning, Philadelphia; Jefferson Medical College of Philadelphia, 1903; member of the Medical Society of the State of Pennsylvania; formerly a druggist; aged 67; died, Dec. 20, 1937, of coronary occlusion.

Frank M. McCafferty ✠ Toledo, Ohio; Ohio Medical University, Columbus, 1895; on the staff of the Toledo State Hospital; at one time demonstrator of obstetrics at his alma mater; aged 71; died, Dec. 14, 1937, of pneumonia.

William Evans, Norfolk, Va.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1890; member of the Medical Society of Virginia; aged 70; died, Dec. 26, 1937, of angina pectoris.

Guy Andrew Darcantel ✠ White Castle, La.; Tulane University of Louisiana School of Medicine, New Orleans, 1900; aged 59; died, Dec. 20, 1937, at the Plaquemine (La.) Sanitarium, of subacute bacterial endocarditis.

John Decker Butzner ✠ Scranton, Pa.; University of Virginia Department of Medicine, Charlottesville, 1904; served during the World War; aged 59; died, Dec. 23, 1937, in the Mercy Hospital, of intestinal obstruction.

Isaac Foster Harter ✠ Stronghurst, Ill.; College of Physicians and Surgeons, Keokuk, Iowa, 1877; formerly druggist, postmaster and member of the board of school trustees; aged 86; died, Dec. 25, 1937, of pneumonia.

Lynn A. Carden, Pelham, Tenn.; University of Tennessee Medical Department, Nashville, 1891; member of the Tennessee State Medical Association; aged 77; died, Dec. 22, 1937, of hypostatic pneumonia.

Harry M. Bunting, Norristown, Pa.; Hahnemann Medical College of Philadelphia, 1879; member of the Medical Society of the State of Pennsylvania; aged 79; died, Dec. 22, 1937, of coronary thrombosis.

Samuel Itscoitz, McKeesport, Pa.; Fordham University School of Medicine, New York, 1915; served during the World War; aged 46; died, Dec. 7, 1937, of arteriosclerosis and cerebral hemorrhage.

Aubrey Russell Greenlee, Kansas City, Mo.; University Medical College of Kansas City, 1892; member of the Missouri State Medical Association; aged 66; died, Dec. 4, 1937, of coronary thrombosis.

Barton T. McDowell ✠ Bristol Center, N. Y.; University of Buffalo School of Medicine, 1892; district director of school hygiene; aged 70; died, Dec. 27, 1937, of heart disease and duodenal ulcer.

Willis Le Forest Gatchell, Stockton, Calif.; Medical School of Maine, Portland, 1882; member of the California Medical Association; aged 82; died, Dec. 31, 1937, of carcinoma of the prostate.

110
938

Murphy M. Morrison, Denison, Texas; Chattanooga (Tenn.) Medical College, 1893; served during the World War; aged 65; died in December 1937, of nephritis and cerebral hemorrhage.

Emmett L. Merrill, Turin, Ga.; Vanderbilt University School of Medicine, Nashville, Tenn., 1890; aged 69; died, Dec. 1, 1937, in the Newman (Ga.) Hospital, of coronary artery thrombosis.

Florence Sharp Manion, Portland, Ore.; American Medical College, St. Louis, 1895; aged 72; died suddenly, Dec. 16, 1937, in the Good Samaritan Hospital, of coronary thrombosis.

Louis Laurenzana ✠ Kansas City, Mo.; Regia Università di Napoli Facoltà di Medicina e Chirurgia, Italy, 1894; aged 67; died, Dec. 11, 1937, in Rome, Italy, of coronary thrombosis.

Myron J. Brooks, New Canaan, Conn.; Rush Medical College, Chicago, 1897; formerly medical examiner and health officer; aged 69; died, Dec. 10, 1937, in Honolulu, Hawaii.

Thomas Teasdale Mutchler, Philadelphia; University of the City of New York Medical Department, 1872; also a minister; aged 87; died, Dec. 13, 1937, of chronic myocarditis.

James William Parsons, Canton, Pa.; University of the City of New York Medical Department, 1880; aged 81; died, Dec. 6, 1937, of organic heart disease and diabetes mellitus.

John Mann Creswell, Searcy, Ark.; St. Louis College of Homeopathic Physicians and Surgeons, 1882; aged 80; died, Dec. 28, 1937, of aortic insufficiency and chronic nephritis.

J. Paul Chambers, Philadelphia; Georgetown University School of Medicine, Washington, D. C., 1884; aged 80; died, Dec. 15, 1937, of chronic myocarditis and arteriosclerosis.

Clarence Carson Parks, Leechburg, Pa.; Jefferson Medical College of Philadelphia, 1906; served during the World War; aged 57; died, Dec. 12, 1937, of coronary occlusion.

Wellington Henry Merriman, Poland, N. Y.; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1895; aged 70; died, Dec. 1, 1937, of acute pyelonephritis.

Oscar Franklin Portwood, Pasadena, Texas; University of Georgia Medical Department, Augusta, 1904; aged 57; died, Dec. 22, 1937, of pneumonia and acute polyarthritis.

Homer Seal McCoy, Sylvester, Ga.; Atlanta Medical College, 1914; member of the Medical Association of Georgia; aged 54; died, Dec. 31, 1937, in an automobile accident.

Walter Henry Darling, Minneapolis; University of Minnesota Medical School, Minneapolis, 1895; aged 64; died, Dec. 6, 1937, in Anoka, Minn., of coronary thrombosis.

Baron Ross Nairn, Buffalo; University of Buffalo School of Medicine, 1895; served during the World War; aged 63; died, Dec. 3, 1937, of carcinoma of the stomach.

William H. Hodges, Watkinsville, Ga.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1890; aged 66; died, Dec. 9, 1937, of heart disease and arteriosclerosis.

Leo Frank Adt, Albany, N. Y.; Albany Medical College, 1892; on the staffs of the Albany Hospital and St. Peter's Hospital; aged 71; died, Dec. 3, 1937, of pneumonia.

Lafayette Noe, Queen City, Mo.; College of Physicians and Surgeons, Keokuk, Iowa, 1897; formerly county judge; aged 69; died suddenly, Dec. 19, 1937, of myocarditis.

J. C. Jones, Buffalo, Ky.; Louisville (Ky.) Medical College, 1889; aged 85; died, Dec. 7, 1937, in Bunnell, Fla., of chronic nephritis, myocarditis and cerebral hemorrhage.

Edward Seymour Moulton, Alameda, Calif.; Yale University School of Medicine, New Haven, Conn., 1894; aged 69; died, Dec. 30, 1937, of nephritis and cystitis.

Thomas C. Harris, Centralia, Va. (licensed in Virginia in 1899); member of the Medical Society of Virginia; aged 61; died, Dec. 6, 1937, of cerebral hemorrhage.

George Sheryl Cabot ✠ Jamestown, N. D.; University of Minnesota Medical School, Minneapolis, 1924; aged 38; died, Dec. 16, 1937, of ventral hernia and ileus.

Alonzo Leaming Bushby, Los Angeles; College of Physicians and Surgeons of Chicago, 1891; aged 71; died, Nov. 13, 1937, of arteriosclerosis and myocarditis.

John Rushing Jackson, Hattiesburg, Miss.; Medical College of Alabama, Mobile, 1890; aged 82; died, Dec. 25, 1937, of coronary embolism and arteriosclerosis.

Carl Herbert Bryant, Atascadero, Calif.; Johns Hopkins University School of Medicine, Baltimore, 1908; aged 56; died, Dec. 22, 1937, of coronary occlusion.

Benjamin F. Cline, Orange, N. J.; University of Virginia Department of Medicine, Charlottesville, 1898; aged 65; died, Dec. 9, 1937, of coronary occlusion.

William Nathaniel Leedom, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1892; aged 73; died, Dec. 11, 1937, of gastric ulcer.

John Burling, Summit, N. J.; Homeopathic Hospital College, Cleveland, 1874; aged 95; died, Dec. 18, 1937, of coronary sclerosis and chronic myocarditis.

Arthur Clinton Helm, Beloit, Wis.; Chicago Medical College, 1884; aged 80; died, Dec. 24, 1937, of cerebral hemorrhage and arteriosclerotic hypertension.

Donald Edmund McKenty, Winnipeg, Manit., Canada; Manitoba Medical College, Winnipeg, 1911; aged 67; died, Dec. 3, 1937, of coronary thrombosis.

Lawrence S. Higdon, Clarkson, Ky.; Kentucky University Medical Department, Louisville, 1905; aged 61; died, Dec. 3, 1937, in an automobile accident.

Frederick Christian Joesting ✠ Alton, Ill.; Washington University School of Medicine, St. Louis, 1901; aged 59; died, Dec. 22, 1937, of heart disease.

John Agnew Hayes ✠ Philadelphia; Temple University School of Medicine, Philadelphia, 1910; aged 67; died, Dec. 12, 1937, of cerebral thrombosis.

Franklin Wiley Lester ✠ Marionville, Mo.; Homeopathic Medical College of Missouri, St. Louis, 1900; aged 68; died, Dec. 14, 1937, of pneumonia.

Maximilian Arthur Auerbach, New York; Illinois Medical College, Chicago, 1899; aged 63; died, Nov. 15, 1937, of tabes dorsalis and pyelonephritis.

John Harrison Fuller, Wichita, Kan.; Kentucky School of Medicine, Louisville, 1881; aged 78; died, Dec. 24, 1937, of carcinoma of the larynx.

William Hiram Mitchell, Boston; Medical School of Maine, Portland, 1899; aged 68; died, Nov. 26, 1937, of coronary sclerosis and thrombosis.

James R. Hawkins, Pelly, Texas; University of Louisville (Ky.) Medical Department, 1881; aged 82; died, Dec. 30, 1937, of cerebral hemorrhage.

George A. Coble ✠ New Augusta, Ind.; Medical College of Indiana, Indianapolis, 1882; aged 76; died, Dec. 31, 1937, of coronary thrombosis.

David W. Cole, Gelatt, Pa.; Baltimore University School of Medicine, 1892; aged 74; died, Dec. 16, 1937, of cardiovascular renal disease.

William G. Korony, Anchorage, Ky.; Hospital College of Medicine, Louisville, 1903; aged 54; died, Dec. 26, 1937, of cerebral hemorrhage.

James Edward Asbury, Los Angeles; Meharry Medical College, Nashville, Tenn., 1882; aged 85; died, Nov. 26, 1937, of chronic nephritis.

Charles Augustin Edelen, Louisville, Ky.; Kentucky School of Medicine, Louisville, 1904; aged 58; died, Dec. 13, 1937, of pneumonia.

Sanders P. Jethrew Lee, Dunn, N. C.; Maryland Medical College, Baltimore, 1904; also a dentist; aged 64; died, Dec. 11, 1937, of uremia.

Charles Lazarus Henkin, Greenpoint, N. Y.; Boston University School of Medicine, 1912; aged 52; died, Dec. 19, 1937, of heart disease.

John Wesley Irvin, Wooster, Ohio; Jefferson Medical College of Philadelphia, 1886; aged 77; died, Dec. 20, 1937, of arteriosclerosis.

Louis Wilhelm Juergens, Milwaukee; Rush Medical College, Chicago, 1888; aged 79; died, Dec. 2, 1937, of chronic nephritis.

Henry Lee Howard, Savannah, Ga.; Southern Medical College, Atlanta, 1881; aged 78; died, Dec. 13, 1937, in a local hospital.

Almon De Bois Gay, Boston; Harvard University Medical School, Boston, 1875; aged 87; died, Dec. 31, 1937, of pneumonia.

Harriet Warner Carman, Los Angeles; Cleveland Medical College, 1892; aged 90; died, Nov. 26, 1937, of chronic myocarditis.

Ida Valeria Beers ✠ Denver; Gross Medical College, Denver, 1901; aged 67; died, Dec. 9, 1937, of chronic myocarditis.

Charles A. Gillette, Brewerton, N. Y.; Albany Medical College, 1883; aged 82; died, Dec. 15, 1937, of pneumonia.

John Ewing, Glendale, Calif.; Chicago Homeopathic Medical College, 1895; aged 70; died, Dec. 21, 1937, of nephritis.

Correspondence

RESUSCITATION OF THE NEW-BORN

To the Editor:—In a communication to THE JOURNAL, January 22, page 304, Prof. Yandell Henderson apparently erred inadvertently as to what constitutes the Flagg technic in initiating respiration in the new-born. This technic is not the insufflation of oxygen deeply into the trachea under conditions which permit a free escape of the gas but is such an insufflation with the escape of the gas so controlled that the lungs are alternately inflated and partially deflated by varying the intrapulmonary pressure caused by the volume of insufflated oxygen (Flagg, P. J.: Art of Anesthesia, ed. 5, p. 391).

The work of Meltzer (THE JOURNAL, May 10, 1913, p. 1407) showed that the blood could be oxygenated without respiratory effort of the subject when the amount of insufflated air or oxygen was sufficiently large. But in all these subjects the lungs had been previously expanded in physiologic use for a long period and during this insufflation the lungs were kept inflated on account of the increased intrapulmonary pressure.

In asphyxia neonatorum, on the other hand, the lungs are collapsed. Aside from respiratory effort of the subject, there has been no way suggested for oxygenating the blood that does not involve an artificial increase in intrapulmonary pressure which expands the collapsed alveoli.

Just how high the intrapulmonary pressure in the infant may be safely raised is a question on which there is a difference of opinion. But as a matter both of information and of caution it may be stated that this is not very high.

RAYMOND C. COBURN, M.D., New York.

COUNTER AND RADIO PRESCRIBING

To the Editor:—In THE JOURNAL, January 22, is an editorial comment on counter prescribing which emphasizes what is common knowledge: that counter prescribing by clerks in drug stores is both flagrant and constant, though many of them have not the excuse (?) of being pharmacists.

No comment has ever been made by any one, to my knowledge at least, of an equally constant and equally flagrant nuisance; namely, "radio prescribing." Many programs, in their commercial broadcasts, recite a varied list of symptoms followed by a recommendation to take the particular product in question according to the directions at once given in detail. Of course, in some few instances there is also a recommendation to see your doctor, which is more than offset by the eminent (though anonymous) group of scientists or "eminent doctors" whose investigations have proved the remarkable value of the product in question.

ROBERT A. KILDUFFE, M.D., Atlantic City.

PRURITUS ANI

To the Editor:—In his article on pruritus ani (THE JOURNAL, February 12, p. 509) Dr. Howard Lilienthal describes a simple cleansing and protective method as commonly prescribed for the anal region by proctologists; this method is not confined to pruritus ani particularly. He suggested that "dirt" or fecal contamination accounted for the so-called pruritus.

The fact that thousands of people under exactly the same conditions as described do not develop pruritus ani is evidence, in my opinion, against his theory.

His simple analysis may be misleading. Pruritus ani is not so simple, as an immense amount of research over many years has disclosed; the condition is a symptom, and the etiology is commonly undiscovered. Allergic manifestations offer much promise in individual cases of identifying the cause. A large percentage of cases of pruritus ani are allergic to the fungi and these are remediable. Food allergic manifestations in the perianal region are not unusual, and a common food is the grape in its various forms, such as wine or brandy. Pruritus ani is an open field for much further investigation.

The modern surgical method of perianal subcutaneous neurotomy which Dr. Lilienthal refers to as a formidable procedure is, when expertly done, very simple, requiring about five minutes. This breaks the vicious circle of itching and scratching, with the resulting secondary infection, and allows such local and systemic treatment as may be indicated.

E. G. MARTIN, M.D., Detroit.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

ALLERGY TO HORSEHAIR

To the Editor:—A boy, aged 4, has had an almost constant watery nasal discharge since he was a few months old, more severe in the winter and when outdoors and when the window of the bedroom is open at night (in winter). When on several occasions he has been close to horses he has reacted with sneezing and conjunctivitis. He has no history of any dermatitis or allergic reactions to any known stimulus. The tonsils and adenoids have been removed. Scratch tests show a reaction to horsehair and to nothing else. There are many articles of furniture in the house containing horsehair. What is the probability of the rhinitis being due to horsehair allergy? If it is not due to horsehair what treatment should be tried? Is horsehair in a mattress or pillow just as potent an allergen as when on a horse?

M.D., Vermont.

ANSWER.—From the history given and the positive scratch test to horsehair it is almost certain that the rhinitis is due to horse dander. Experience has shown that a positive test to horse dander is very apt to be associated with clinical symptoms. This is especially true when the positive reaction is by the cutaneous or scratch method, as this method, when positive, indicates a much greater degree of hypersensitivity than the intradermal method of testing. Treatment should consist of as rigid avoidance of horse dander as is possible; all horsehair in the house should be removed; the contents of couches, mattresses, pillows and carpet pads should be investigated; some long hair brushes are made of horsehair. Felt hats, automobile paddings, colt and pony skins and manure must also be considered. It is, of course, essential to avoid horses, horse shows, stock shows and polo games; residence near a stable may be associated with sufficient exposure to cause symptoms. Sensitive individuals must avoid not only horses and stables but also all persons or objects, such as a riding-habit directly or indirectly connected with the handling of horses.

Hyposensitization to horse dander would seem advisable, as it is almost impossible to avoid horsehair and horse dander completely. If avoidance does not remove symptoms in a few weeks the child should be given injections of an extract of horse dander. The initial dosage should be small, perhaps 0.1 cc. of a 1:1,000,000 extract; increases should be gradual, from 40 to 50 per cent each dose; local reactions demand caution. The top dosage varies, but many patients can reach a 1:1,000 or a 1:100 dilution with safety and good results.

Horsehair in a mattress or pillow, if properly sterilized, should not be as potent an allergen as when on a horse, and yet it is impossible to destroy an antigen completely except by a more prolonged sterilization than is customary, nor can one wash all the dander out of horsehair. Therefore horsehair mattresses can cause symptoms in all but the least sensitive individuals. Cold air or exertion may aggravate symptoms.

It might be well also to caution against the use of horse serum in this child, as almost all individuals who are sensitive to horse dander are sensitive also to horse serum. The use of diphtheria and tetanus antitoxin should call for extreme caution. Precautions can be found in any textbook on allergy.

110
938

PAIN IN HIP AND LEG

To the Editor:—Can you suggest treatment for an intractable case of what has been provisionally diagnosed as toxic neuritis and fibrositis of the lower limb? The patient is 73 years of age. Pain in the hip first began in January 1937 and was accompanied by pain in the right humerus. The prostate was enlarged but there was no residual urine. In view of the possibility of malignancy, a complete examination was made, including x-ray examination of the long bones and pelvis, but everything was normal. The basal metabolic rate was —10. Prostatectomy was performed in two stages, the second operation three weeks after the first. The patient was discharged from the hospital eight weeks later, with healthy bladder and a full stream of urine. The pathologic report was that there were two fibro-adenomatous growths in the prostate and no malignant condition. During the time the bladder was draining there was no pain in the limb, but when drainage ceased and the suprapubic wound healed pain returned with increased intensity and now after two months the pain is as severe as ever, so that there is no rest at night. Temporary relief can be obtained by sitting up. The nature of the pain is that it recurs in waves of intensity in the gluteal region and from the knee to the ankle, over the region supplied by the external popliteal nerve. The muscles are sensitive in this region and the cutaneous reflex is increased. The skin is sensitive to the sun's rays, which cause erythema and severe itching. A half minute's exposure to the quartz lamp at a distance of 25 inches caused a severe reaction. The neurologist's report of the nervous system is negative except for the limb. The only x-ray evidence is an old arthritis of the lumbar spine, and productive change in the first and second lumbar vertebrae with a bony bridge joining the two, but that condition has been present for ten years without inconvenience. The treatment so far adopted has been fifteen minutes daily with the inductotherm for a week, infra-red application, the quartz lamp for two applications and a superimposed wave (McIntosh machine) five minutes daily for a week, with high voltage roentgen therapy over the lumbar spine for eight daily treatments, each being for six minutes at 50 cm., 20 milliamperes, filtered through 1 mm. of copper and 3 mm. of aluminum. The x-rays seemed to give some relief but all other treatments failed. Massage seemed to help. I should be glad of any suggestions that might help.

M.D., Newfoundland.

ANSWER.—The treatment thus far instituted is empirical and is carried on in line with what would be recommended for fibrositis, neuritis and arthritis. The fact that the x-rays seem to give the most relief may be of some significance. Pain from a malignant growth is usually relieved temporarily by roentgen treatment. Unfortunately, some patients on whom prostatectomy has been done, although no malignant condition could be demonstrated in the specimen, have later died of multiple metastases to the bone. This must not be lost sight of in this patient.

Treatment will have to be symptomatic, with such drugs as are necessary to relieve pain; but opiates should be avoided as much as possible. If the pain should be due to a malignant condition it will become steadily worse and opiates will have to be used in increasing amounts. Therefore they should be administered only when really needed. If the dose is increased, not only will the patient suffer from the systemic effects of large doses of the narcotic but a tolerance to the drug will develop and the pain will not be controlled even by huge doses. It is extremely unlikely that the pain would have been caused by any damage occurring from the spinal anesthetic.

ASCENDING NEURITIS

To the Editor:—The tenth edition of Osler's Practice of Medicine states on page 1050: "A neuritis limited at first to a peripheral nerve may extend upward—the so-called ascending or migratory neuritis—and involve the larger nerve trunks or even reach the spinal cord—causing subacute myelitis (Gowers). The condition is rarely seen in the neuritis from cold or in that which follows fevers; but it occurs most frequently in traumatic neuritis." Is this statement regarded as true? All the neurologists I have spoken to about this deny that such a thing is possible. Kindly supply me with references.

M.D., New York.

ANSWER.—Gowers (A Manual of Diseases of the Nervous System, vol. 1, Diseases of the Spinal Cord and Nerves, London, J. & A. Churchill, 1886): "'Migrating neuritis' is not rare in man and is readily produced in animals. It may reach the spinal cord and there produce various disturbances. The inflammation may spread in the tissues outside the dura mater or may extend to the cord and cause subacute or chronic myelitis with or without meningitis" (p. 57). The condition is much rarer, however, than Gowers supposed. Oppenheim (Textbook of Nervous Diseases for Physicians and Students, ed. 5, translated by Alexander Bruce, vol. 1, London and Edinburgh, T. N. Foulis, 1911) says: "The neuritis ascendens or migrans, which plays a great part in earlier literature, is rare. Experimental investigations have shown that an artificially produced suppurative inflammation of the nerves may ascend along the nerve and may advance intermittently in a centripetal direction" (p. 419). In a footnote Oppenheim states: "In the great majority of cases shown to me as ascending neuritis, I have found that there was not a neuritis but a traumatic neurosis or hysteria; there were only two or three in which a true ascending neuritis seemed to exist, as in one case in which a musculospiral paralysis followed a slight wound of the finger." In this case, however, influenza had also previously been present. In general, the French neurologists Dejerine and Raymond upheld the position of an infective form of ascending neuritis, which even reached the spinal cord.

Up to the time of the World War, therefore, ascending neuritis was certainly rarely found, although occasionally traumatic cases have been described. Tinel (Nerve Wounds: Symptomatology of Peripheral Nerve Lesions Caused by War Wounds, New York, William Wood & Co., 1917), who had a large experience with peripheral nerve lesions, found definite cases, although the condition was rare. The condition is characterized "by the fact that the traumatized nerve not only degenerates rapidly toward its peripheral extremity but undergoes a slow, progressive, ascending degeneration of its central segment" (p. 81). He found that it was most frequently the result of a focus of bony suppuration. When the condition is severe, it usually continues for months and sometimes years, seldom stopping before reaching the plexus and the spinal cord itself. Tinel found that section of the nerve above the lesion, or even amputation of the limb itself, was not always sufficient to stop the process, if the infectious or toxic agent had already gone beyond the point of section. Tinel was baffled by the exact nature of the condition and felt that no form of treatment was satisfactory.

According to Wilfred Harris (Neuritis and Neuralgia, Humphrey Milford, Oxford University Press, 1926), a similar condition is occasionally found in diphtheria when, for instance, the navel of a new-born infant has become infected. Neuritis develops in the neighboring nerves and it seems probable that the toxin travels along the perineural lymphatics, as demonstrated experimentally by Orr and Rows. Ascending neuritis, moreover, according to Harris, is seen also in leprosy. The condition is well recognized surgically and a good description will be found in Homans' textbook (A Textbook of Surgery, ed. 4, Springfield, Ill., and Baltimore, Charles C. Thomas, 1936), page 295. He too speaks of the severe nature of the condition and the difficulty of cure.

It would seem, therefore, that ascending or migratory neuritis, once considered fairly common, is really a rare disease. Cases, however, have been observed, particularly during the World War, which have led to the recognition of this condition in neurologic literature. Some of the current textbooks, however, do not mention ascending neuritis. Incidentally, the statement quoted from the tenth edition of Osler's Practice of Medicine has remained unchanged in the twelfth edition, 1935.

EFFECTS OF INADEQUATE TREATMENT OF PRIMARY SYPHILIS

To the Editor:—My impression is that insufficient treatment for syphilis, for example, six intravenous injections of an arsenical given during the primary stage, has a tendency to influence the disease to skip the secondary stage and pass on to the third stage or to the central nervous system. Is there a tendency likewise for the six injections to influence the disease not to involve the vascular system and jump to the central nervous system? In other words, would you consider aortitis as an intermediary between the secondary stage and involvement of the central nervous system or is aortitis an end result of the third stage? Another way of expressing the question would be, Would a person who does not have any treatment have more chances of having aortitis and not having the central nervous system involvement than one who has only six injections? It is true, is it not, that a person with vascular syphilis rarely has syphilis of the central nervous system?

M.D., Mississippi.

ANSWER.—Six doses of arsphenamine given during the preliminary stage of syphilis, far from influencing the disease to skip to the secondary stage, would probably provoke a higher incidence of infectious mucocutaneous relapse of the secondary type than if no treatment had been given. There is no satisfactory evidence that the inadequate treatment of early syphilis, whether primary or secondary, increases the incidence of any type of central nervous system syphilis, except acute meningeal neurosyphilis, although such inadequate treatment may hasten by several years the appearance of clinical symptoms and signs of all forms of neurosyphilis. There is gradually accumulating evidence to indicate, however, that even the thoroughly inadequate arsenical treatment of early syphilis is of value in reducing the ultimate incidence of syphilitic aortitis. Thus the inadequate treatment of early syphilis may increase the incidence of infectious mucocutaneous relapse and of acute meningeal neurosyphilis; has no influence on the incidence of other forms of neurosyphilis except to hasten the time of appearance of clinical symptoms and signs, and may protect the patient against the ultimate development of cardiovascular syphilis.

Aortitis is not an intermediary between the second stage and involvement of the nervous system. From the pathologic standpoint, invasion of the aorta probably occurs quite early in the course of the disease. From the clinical standpoint, however,

the development of cardiovascular syphilis is an event of late syphilis with an average interval of approximately twenty years between infection and the appearance of clinical symptoms and signs.

A person who does not have any treatment does run more chance of the development of aortitis than one who has had only six injections in the primary stage. The absence of early treatment, however, does not render him less liable to the development of central nervous system involvement than inadequate early treatment.

It is distinctly not true that a person with vascular syphilis rarely has neurosyphilis. On the contrary, the two conditions are associated with a high degree of frequency.

REACTION TO DIGITALIS

To the Editor:—A woman, aged 50, has cardiovascular syphilis and exhibits signs of aortic regurgitation and aortic stenosis, enlargement of the heart, and syphilitic aortitis with a beginning fusiform aneurysm. Also she has eczema of the external auditory canals. Her blood pressure varies from 210/80 to 130/80, most of the time being around 175/80. Since February 1937 I have given her 2 cc. of iodobismitol each week. In May the patient began to have edema of the ankles and feet and of the abdominal wall. Her pulse was 100 and regular. I gave her 1½ grains (0.1 Gm.) of digitalis three times a day. Six days later she had nausea and vomiting. Her pulse was 48 at the precordium, at the vessels of the neck and at the wrist. It was slightly irregular. I took her off digitalis and she made a rapid recovery. Eight days later I resumed the digitalis with a dosage of 1½ grains daily. Twelve days later she again had nausea and vomiting. The pulse rate was 70 and regular. I stopped the digitalis and after she recovered, thinking that I was dealing with gastric irritation, I had some rectal suppositories of digitalis 3 grains (0.2 Gm.) made up and gave her one twice a day for three days and then one daily. Nine days later the patient was again vomiting. The pulse was 70 and regular. Thinking that possibly the patient had a digitalis "fixation" I let her think I was giving her some "nerve" pills but actually gave her 1½ grains of digifoline three times a day. Two days later the patient developed urticaria and on the following day began to vomit again. I am aware that digitalis is not well tolerated in cases of aortic regurgitation, but I am not aware of the reason. Is it possible that the patient could be allergic to digitalis? May not the urticaria have been a sign of this? Would 1 cc. of digalen or digifoline or one of the other injectible digitalis preparations given intradermally serve as a skin test? And could the patient be desensitized if allergy exists by increasing doses of the same preparation?

M.D., Iowa.

ANSWER.—The symptoms described do not suggest an allergic sensitization to digitalis. They are definitely the symptoms of the pharmacologic effects of digitalis. The urticaria in this case, occurring as it did after many days of the administration of digitalis, is not at all a likely indication of an allergic reaction. It is much more likely a coincidental occurrence.

This patient apparently responds normally to digitalis but requires much smaller doses to produce slowing of the heart. It is necessary in such a case to administer smaller doses, to watch carefully for the first signs of nausea or pulse irregularity, and to reduce the dose as soon as these signs become manifest. With the occurrence of the toxic symptoms described it may be necessary to wait not nine days but a full three weeks before resuming digitalis therapy at a reduced dosage.

ELECTROLYSIS—REMOVAL OF HAIR

To the Editor:—What is the difference in chemical reaction when the needle is inserted in a hair follicle to remove superfluous hair, first if the positive pole is used and secondly if the negative pole is employed? A black dot is left if the positive pole is employed; this occurs immediately after the electricity has been turned on. Is there any treatment to remove this black dot? What is to be done if the spot does not disappear?

M.D., New York.

ANSWER.—The principle of electrolysis can be demonstrated by plunging two platinum wires, connected with the positive and negative poles of a galvanic current, into acidulated water. These should be kept a small distance apart. On closing the circuit the water is decomposed into its component gases, the electropositive element, hydrogen, is liberated at the negative pole; the electronegative element, oxygen, is found at the positive pole.

When the positive pole is used, the reaction of the tissue, as the result of the liberated oxygen, is acid.

When the negative pole is inserted into living tissue the reaction of the tissue is alkaline, owing to the liberation of hydrogen. Albumin is coagulated.

For this work very fine iridioplatinum or unoxidizable steel needles should be used for positive pole work. For negative pole work, platinum or plain steel needles may be used.

The black dot is due to formation of a perchloride of iron when plain steel needles are used with the positive poles. This is a form of tattooing and should be treated on the same principles.

SPONTANEOUS PNEUMOTHORAX

To the Editor:—A youth, aged 18 years, an experienced French horn player, suffered a complete spontaneous collapse of the right lung ten weeks ago while playing his instrument. Previously, in the spring, while in the orchestra, he felt momentary pain in the right side of the thorax and transient dyspnea. No physician saw him at these times. Following the collapse there was slight fever for two or three days and considerable dyspnea with displacement of the mediastinal contents. The air was absorbed in three or four weeks; a small amount of fluid formed, and, on absorption of the fluid, there was some pleural pain for a few days. The Mantoux test (0.1 cc. of 1:1,000 old tuberculin known to produce positive reactions) was negative, and stereoroentgenograms after expansion showed no abnormalities. He is in excellent health now. Would it be advisable for the boy to return to horn blowing, and if so how soon? He is more or less dependent on his music to obtain a college scholarship and is anxious to continue playing if there is no great additional risk.

M.D., North Carolina.

ANSWER.—In recent years, through modern methods of diagnosis and periodic examinations of healthy persons, spontaneous pneumothorax has been removed from the list of rare conditions. While it is true that many pathologic processes, such as tuberculosis, malignant growths, pneumonia and abscess, may cause spontaneous collapse, the fact is now well established that many persons have this condition in whom the most complete examination fails to reveal any evidence of disease in the lung during life.

The condition described was designated "pneumothorax simplex" by Kjaergaard (*Acta med. Scandinav.* **43**:17), who called attention to the fact that it occurs in healthy persons and frequently has no relationship to tuberculosis. Prior to his work, spontaneous pneumothorax was regarded as prima facie evidence of tuberculosis and not less than one year of strict bed rest preferably in a sanatorium was recommended. Further investigation, however, has revealed the fact that even the tuberculin test is negative in many young adults with spontaneous pneumothorax. In fact, in some groups of cases with undetermined etiology, such as those reported by Leggett, Myers and Levine (*Am. Rev. Tuberc.* **29**:348 [March] 1934), more than 50 per cent were negative to the tuberculin test. Pneumothorax simplex appears with much greater frequency among young males than among females of the same age, but no satisfactory explanation has been offered for this difference in the sexes. The French have referred to it as "pneumothorax des conscrits," as they have seen it most frequently in men of military age, from 20 to 40. It is thought that pleural blebs or congenital cysts may be responsible for many such cases. As pathologic areas in the lung or pleura must be macroscopic and favorably located to be brought to light by x-ray examination, it is impossible to determine the location of the rupture in the visceral pleura during life. The use of the thoracoscope may be helpful, but even this method does not always locate the area.

The symptoms of pneumothorax simplex usually consist of excruciating pain in the chest, which may persist for a few minutes and gradually subside. Often this is accompanied and followed by a period of dyspnea, which in most cases is severe for a short time and within a few hours has almost completely disappeared. The condition may develop during some exertion, such as lifting or carrying a heavy load, violent laughter, coitus, and straining at stool; again, it may occur when the patient is sitting quietly in a chair and it has even been reported to occur during sound sleep. In most cases of pneumothorax simplex, apparently the rupture in the visceral pleura soon closes and the air in the pleural cavity slowly absorbs, so that within a few weeks the lung completely reexpands. It is not uncommon to see a small amount of serous fluid accumulate in the pleural cavity. Usually no treatment is indicated if a diagnosis of pneumothorax simplex is definitely established. Until such a diagnosis is established, however, it is well to have the patient on strict bed rest while the lung is observed to be reexpanding in the usual manner.

Spontaneous pneumothorax may appear on the two sides simultaneously; again, the condition may exist on one side and at some subsequent time appear on the opposite side. Recurrent spontaneous pneumothorax has been reported by a number of physicians, but apparently many persons who have pneumothorax simplex never have recurrences regardless of occupation or activities; at any rate they do not report to physicians.

The examination of this patient was adequate to rule out tuberculosis and probably has eliminated other serious lung disease. It is impossible to determine whether there will be one or more recurrences regardless of whether he plays a wind instrument, as spontaneous collapse might recur even while he is sleeping. Again, there may never be a recurrence even though he continues as a musician or indulges in violent exercise. However, as there is the remote possibility of complications, such as empyema, in case of recurrence, it would seem safer to have him avoid strenuous exertion.

LICE

To the Editor:—Is it possible to have recurrent attacks of infestation with Pediculus pubis over a period of five years—say every year and a half or so? Is there a spore or some part of its life cycle that can burrow deeply and come to the surface at the time? I have a patient who has had three attacks within the last eight years, the last attacks about two years or less apart. He is meticulous about his linen and bathing habits. He is firm in his denial of sexual intercourse outside his home. In cases of intercourse with an infected partner, after how long a time will the infection be noticed by the free partner? In other words, if he had outside intercourse say three months ago could he be just noticing the infestation? Each infestation (which has been light, from three to six lice actually found) has been treated with thorough shaving and mild mercurial ointment.

M. W. NEW, M.D., Seoul, Korea.

ANSWER.—Lice do not sporulate but lay eggs, called nits, which appear as pear shaped white bodies tightly adherent to the hair. They hatch in from four to seven days and cannot lie dormant. A new attack of pediculosis can be acquired only by another infestation. Sexual contact is not necessary. Lice can be acquired from infected clothing or bed linen.

The time elapsing between infestation with the crab louse and their coming to the attention of the host depends on his power of observation. The fact that the crab louse does little traveling and hangs with its head in the follicular opening makes it much less easily seen than other lice; but the itching is usually intense and should prevent the host from remaining ignorant for very long of the presence of his guests. It is possible that there are persons who do not experience much itching; but that a man of cleanly habits could harbor these parasites for months without being conscious of their presence is highly improbable.

It is a well established fact that certain persons are very attractive to lice, so that they readily leave another host. It may be that the patient mentioned is one of these.

A solution of mercury bichloride in water, 1:500 or even 1:250, is just as efficient as the mild mercurial ointment and much less messy. Shaving should be thorough, so that no nits escape. The hair on the abdomen, thighs, lower part of the back, chest, axillae and even the eyelashes and the hair at the border of the scalp should be inspected for nits.

ULNAR NEURITIS FROM INFECTION

To the Editor:—I have recently treated two patients who gave similar histories. One had a splinter in the web between the middle and ring fingers. This was followed by infection of moderate degree, without an associated lymphangitis, lymphadenitis or fever. Neither the hand nor the forearm was immobilized other than for the dressing of the fingers. About ten days later a beginning atrophy of the first interosseous muscle was noted, which has progressed for a period of a year, so that there is practically no muscle tissue remaining. The second patient also had a splinter in the web between the ring and little fingers. This hand has been immobilized for a month. The atrophy he is showing is more generalized, involving all interossei. The first patient was examined by a neurologist, who felt that he had developed an involvement of the ulnar nerve. What may the connection between the injury and subsequent infection be? If there is an ulnar paralysis, what part of this nerve was involved in such a way that other features of ulnar palsy are absent?

M.D., New York.

ANSWER.—The symptoms described can be accounted for by ulnar neuritis resulting from the infection. The deep branch of the ulnar nerve, which controls the motor trophic function of the interosseus muscles, crosses the palm from the ulnar to the radial side to end in the first dorsal interosseus, the adductors of the thumb and the medial head of the short flexor of the thumb. The difference in involvement in the first and second cases can be explained by the fact that in the first case the involvement was closer to the termination of the nerve and a shorter segment of the nerve was involved. In the second case the involvement was more proximal and the fibers of innervation to all the interossei were affected. It is probable that the sensory fibers of the ulnar nerve, which separate from the nerve trunk close to the level of the pisiform bone, escaped injury and therefore the typical area of anesthesia associated with injury of the ulnar nerve above the wrist is lacking.

PAIN TO CHILD DURING DELIVERY

To the Editor:—Does the child that is being born suffer pain at any time during its expulsion from the interior of the uterus. Can you refer me to any researches on this point?

M.D., Missouri.

ANSWER.—This question has been considered to some extent and references can be made to the articles by Peterson and Rainey (*Bull. New York Lying-in Hosp.*, December 1910), Pratt, Kraushaar and Sun (Behavior of New-Born Infant, Ohio State University Press, Columbus, 1930) and Canestrini (Sinnesleben des Neugeboren, Berlin, Julius Springer, 1913).

It is known that a baby will draw its hand away when one tries to touch it in utero and will wriggle his head away from pressure during a vaginal examination. He changes his position frequently, evidently for comfort.

During actual delivery the baby probably suffers pain, because as soon as he gets out he cries vigorously and if pinched will cry some more.

Babies live in the uterus and during labor in a state of suboxidation or partial anoxemia, which probably makes them torpid. It is more than possible that the first vigorous cry is the result of the pain of labor. F. F. Snyder has shown that in rabbits respiration with circulation of liquor amnii in the lungs continues throughout the latter part of pregnancy and there is reason to believe that the human fetus has respiratory action during pregnancy. If this turns out to be the rule there will be no necessity for the various theories regarding the cause of the first respiration; the baby simply continues as it was in utero. Perhaps the first cry may be explained by the pain which the baby suffers during delivery.

SNAKE VENOM

To the Editor:—A patient has the unique hobby of studying and handling snakes. Among those with which he deals are water moccasins, copperheads, rattlesnakes and corals. In addition, he is planning on adding to his collection by an early visit to the Everglades. Naturally, he is cognizant of the danger to which he is exposed and as a result would like to know the feasibility of active immunization. Is this possible? If so, how efficient is this procedure? Is there any appreciable danger? How permanent is the immunity (if any)? Is there sufficient similarity in the toxins to give rise to multiple immunity from the antigen?

M.D., New York.

ANSWER.—It is probable that immunization against the common poisonous snakes is not practical. After one month of injections a venom used in this manner contained anaerobic and aerobic organisms. Later both tetanus and gas gangrene organisms were found in similar venom. Dr. Githens at the Mulford Biological Laboratory reports extensive liver and kidney damage in horses used in the manufacture of antivenin. In preparing antivenin, multiple antigens are used.

A snake collector is advised to wear boots, use great care, equip himself with a suction first aid kit and study the directions carefully before entering the field. If antivenin is carried, not less than five syringes are advised.

SUCCESSFULNESS OF SKIN GRAFTS

To the Editor:—I shall appreciate statistics regarding percentage of takes of various skin grafts employed in treatment of third degree burns of the leg.

M.D., Illinois.

ANSWER.—Accurate statistics on the percentages of takes of the various types of skin grafts used in the treatment of third degree burns of the leg are difficult to state for the reason that the condition of the wound, the skill of the surgeon, and judgment as to type of grafts and of dressings used varies so much.

In the hands of an experienced surgeon with the granulations in perfect condition, small deep grafts on the leg will take practically 100 per cent; Ollier-Thiersch grafts will take approximately from 80 to 90 per cent. Whole thickness grafts in these cases are ordinarily contraindicated.

GIARDIA LAMBLIA AND CHILOMASTIX MESNILI

To the Editor:—Can you give me information on the treatment for elimination of Giardia lamblia, and also of Chilomastix mesnili? While I realize that these organisms are non-pathogenic, I have lately had more than one case of chronic recurring diarrhea. Repeated stool examinations have shown decidedly more than usual presence of Giardia. I have also one case in which Chilomastix mesnili is in abundance with similar symptoms. The patient I have in mind at present is a child about 10 years of age. I have tried carbarsone in the hope that it might have some effect in eliminating the symptoms, without any results. I would greatly appreciate any information you may be able to give me.

W. R. HERBERT, M.D., San Diego, Calif.

ANSWER.—Giardia lamblia inhabits the duodenum and upper jejunum and has been found in the gallbladder. It is therefore not easily accessible to any form of chemotherapy. Sometimes treatment with amebacidal drugs such as carbarsone and chiniofon have been followed by its elimination, but the treatment is uncertain. Chilomastix mesnili inhabits the cecum and colon and sometimes the lower part of the ileum. Elimination of sugar from the diet and the restriction of other carbohydrates will sometimes cause elimination of the infection or the cessation of symptoms. Carbarsone has proved effective in some cases. The presence of these parasites is so common in the absence of clinical symptoms that some other cause for the symptoms should always be sought.

TRAUMA AND LANDRY'S PARALYSIS

To the Editor:—Please discuss the etiology of acute ascending paralysis (Landry's). A man, aged 22, had a minor laceration of the head from a fall in a coal mine. Three or four weeks later he complained of mental symptoms. In the hospital roentgenograms were taken of the skull and the entire vertebral column but showed nothing abnormal. This case will come before the referee simply because of the head injury. Please advise me whether it is remotely possible that a minor laceration of the scalp could be the cause for this paralysis. I should like to have something definite, so that should I be asked the question about the blow or laceration being the cause I shall be able to answer correctly.

M.D., Pennsylvania.

ANSWER.—There is no actual evidence that trauma plays any part in Landry's paralysis. Although the disease cannot be considered as a definite entity, the syndrome has many causes and some cases closely resemble acute polyneuritis while others suggest poliomyelitis. Occasionally rabies takes the form of acute ascending paralysis and, more rarely, multiple sclerosis. Trauma of the scalp, as described, cannot in any way be associated with this disease.

BETTS AND SNELLEN CHARTS IN REFRACTION

To the Editor:—I have advised against the adoption of the Betts test in the public schools in my neighborhood. What is the opinion regarding the usefulness and accuracy of this test? It seems to me that a child whose eyes need attention will show defective vision by the ordinary Snellen chart or symptoms in relation to the use of the eyes. Further analysis of these symptoms is the function of the eye physician. The agent who called on me showed me an article in THE JOURNAL of Jan. 11, 1936, page 147, in which the general tone of the remarks was favorable.

WENDELL L. HUGHES, M.D., Hempstead, L. I., N. Y.

ANSWER.—The Betts charts are not considered by most ophthalmologists as superior to the Snellen chart. The latter remains the standard in testing vision and is probably more accurate than any other test. The diagnosis of refractive errors by the Betts charts is exceedingly unreliable and in the hands of nonmedical examiners is likely to lead to error and misunderstanding. The presence of binocular vision can be determined by the charts, but this is of doubtful value unless correlated with other observations of the eye physician who has other means as good for determining this function.

EFFECT OF ALCOHOL ON TOXICITY OF PROCAINE

To the Editor:—Kindly advise as to the possibilities of increased toxicity of procaine hydrochloride by admixture with ethyl alcohol in small amounts.

M.D., Indiana.

ANSWER.—Ethyl alcohol, even in a small amount, is likely to increase the toxicity of procaine hydrochloride. It will do this by increasing its penetration into tissues as well as absorption into the blood.

GASTRIC PHOTOGRAPHY

To the Editor:—In THE JOURNAL, Dec. 11, 1937, page 2008, appears an inquiry regarding the use of the gastrophotor, a camera for the photographing of the interior of the stomach. During eight years I have taken intragastric photographs in more than 300 cases. My latest paper on the subject, which covered 216 cases studied at the Beth-El Hospital, was published in the *American Journal of Digestive Diseases and Nutrition* (3: 155 [May] 1936, abstr. THE JOURNAL, July 25, 1936, p. 309). Roentgenology is the most valuable single method in use for the diagnosis of gastro-intestinal lesions. There are some gastric conditions, however, in which the roentgenogram fails to show the presence of any lesion or only a suggestive sign of a lesion. Such is the case usually when the lesion is located on the posterior wall of the stomach or when the ulceration is shallow and superficial. In such cases gastrophotography is of value. The gastroscope is being used at present also for the diagnosis of gastric lesions. However, special training is necessary and it is a time consuming procedure objectionable to many patients. The use of the gastrophotor with the improved camera is a simple procedure taking only about thirty seconds to photograph a stomach. Its introduction is not more difficult than introducing a stomach tube for an ordinary Ewald test meal. In addition, intragastric photographs have advantages that are common to roentgenologic films, metabolism charts and other graphic presentations; namely, they are picture records, in permanent form, to be examined and studied at the leisure of the physician and can be compared with subsequent examinations. The three specific adverse points made in your reply can easily be refuted by any one who has studied the published reports and the Scientific Exhibits at the 1935 and 1937 sessions of the American Medical Association: 1. It is the opinion of many physicians who have worked with the gastrophotor that the pictures are clear and may be readily interpreted after some experience. These pictures are actual photographs and therefore show the gross pathologic changes present in the stomach. 2. By proper technic a correct orientation of the stomach is obtained. 3. Important changes in the mucosa are reproduced even on the black and white films. The last mentioned fact can be demonstrated by any one who will take the trouble to study the films and compare the pictures with the actual conditions found in the specimens obtained after surgical resection or postmortem examinations.

REUBEN FINKELSTEIN, M.D., Brooklyn.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

Examinations of state and territorial boards were published in THE JOURNAL, March 5, page 761.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I and II.* Examinations will be held in all centers where there is a Class A medical school and five or more candidates who wish to write the examination, May 9-11 (limited to a few centers), June 20-22, and Sept. 12-14. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

SPECIAL BOARDS

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGY: *Written examination for Group B applicants* will be held in various cities throughout the country April 16. *Oral examinations for Group A and B applicants* will be held at San Francisco, June 13-14. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *General oral, clinical and pathological examinations for all candidates (Groups A and B)* will be conducted in San Francisco, June 13-14. *Application for admission to Group A examinations must be on file before April 1.* Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6).

AMERICAN BOARD OF OPHTHALMOLOGY: San Francisco, June 13; Washington, D. C., Oct. 8; Oklahoma City, Nov. 15. *All applications should be filed immediately and case reports, in duplicate, must be filed not later than sixty days before the date of examination.* Sec., Dr. John Green, 3720 Washington Blvd., St. Louis, Mo.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Chicago, June 10-11. Sec., Dr. Fremont A. Chandler, 6 N. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: San Francisco, June 10-11. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF PEDIATRICS: New York City, May 3-4 and San Francisco, June 12. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: San Francisco, June 11. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: San Francisco, June 10-12. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF UROLOGY: San Francisco, June 11-13. *All condensed case reports must be filed by April 1. Written examination* will be held in various cities in the United States and Canada, April 2. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

Arkansas December Examination

Dr. L. J. Kosminsky, secretary, State Medical Board of the Arkansas Medical Society, reports the written examination held at Little Rock, Dec. 21-22, 1937. The examination covered 12 subjects and included 120 questions. An average of 75 per cent was required to pass. Three candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Arkansas School of Medicine		(1937)	85.1, 85.4
Tulane University of Louisiana School of Medicine		(1931)	87.6

Eleven physicians were licensed by reciprocity and two physicians were licensed by endorsement from July 29 through December 23. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Illinois College of Medicine		(1936)	Illinois
University of Kansas School of Medicine		(1934)	Kansas
Louisiana State University Medical Center		(1937)	Louisiana
University of Michigan Medical School		(1929)	Penna.
Memphis Hospital Medical College		(1908)	Tennessee
Univ. of Tennessee College of Med. (1920), (1930), (1934) (1936)			Tennessee, Louisiana
Vanderbilt Univ. School of Medicine		(1916)	Texas, (1934) Tennessee

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Johns Hopkins University School of Medicine		(1935)	N. B. M. Ex.
Temple University School of Medicine		(1934)	N. B. M. Ex.

Connecticut (Homeopathic) November Examination

Dr. Joseph H. Evans, secretary, Connecticut Homeopathic Medical Examining Board, reports the written examination held at Derby, Nov. 9-10, 1937. The examination covered 7 subjects and included 70 questions. An average of 75 per cent was required to pass. Two candidates were examined, both of whom passed. The following school was represented:

School	PASSED	Year Grad.	Per Cent
Hahnemann Med. College and Hospital of Philadelphia		(1937)	82.4,* 82.5*

*License has not been issued.

Book Notices

Clinical Parasitology. By Charles Franklin Craig, M.D., M.A., F.A.C.S., Professor of Tropical Medicine in the Tulane University of Louisiana, New Orleans, and Ernest Carroll Faust, M.A., Ph.D., Professor of Parasitology in the Department of Tropical Medicine, Tulane University of Louisiana, New Orleans. Cloth. Price $8.50. Pp. 733, with 243 illustrations. Philadelphia: Lea & Febiger, 1937.

This book, by two of America's greatest experts in parasitology, belongs in the library of every practicing physician. To a considerable extent the rapid growth of bacteriology and its applications to medicine have overshadowed its sister science parasitology, with the result that the latter has not received the attention it fully deserves, particularly in temperate climes. In the face of repeated warnings in the medical literature over a period of years indicating that amebiasis, for instance, occurs throughout the United States with an average incidence of 10 per cent, realization of the importance of this disease in clinical medicine is only beginning to be appreciated. Knowledge of the methods of detection of Endamoeba histolytica and of its differentiation from harmless protozoa is not yet part of the equipment of the average clinician or even of many pathologists. Methods of preventing the disease are not widely known; the role of polluted urban water supplies in the transmission of the disease has been largely ignored. As the authors point out, ". . . it should be remembered that [polluted] water can be rendered safe only by boiling or filtration, as chlorine or other chemicals used in water purification are useless, owing to the resistance of the cysts of E. histolytica to these agents." In addition, adequate methods of treatment, though several are available, are often poorly understood. The remarkable progress that has been made in the elimination of hookworm infestation in the southern part of the United States is an excellent example of the cooperation of clinical and preventive medicine in the conquest of a parasitic disease. Proper utilization of the information in this book should go far toward the elimination of other infestations, among which amebiasis is one of the most widespread and most important. Among the subjects considered in the text are pathogenic and nonpathogenic amebas, intestinal, blood and tissue flagellates, coccidia, malarial plasmodia, ciliates, trichinella, trichocephalus, strongyloides, hookworms, ascaris, filaria, flukes, tapeworms, crustacea, millipedes, centipedes, spiders, ticks, lice, flies, blood-sucking flies, mosquitoes, fleas, bees, wasps and hornets. Especially valuable is a detailed technical appendix which includes methods of collection, preparation and identification of various parasites. The authors have incorporated an extensive and well chosen bibliography. Professors Craig and Faust are to be congratulated on the preparation of a comprehensive, unusually well organized, scientific and practical treatise. The book is excellently printed and profusely illustrated with drawings and photomicrographs.

Le cancer ulcériforme de l'estomac (étude clinico-radiologique). Par le Docteur Th. J. Péristiany. Paper. Pp. 113, with 44 illustrations. Paris: Librairie E. Le François, 1937.

This small volume represents a thesis in monograph form, embracing a clinical and radiologic study of an important and controversial topic. The investigation was carried out under the encouragement and guidance of Professor Gosset, chairman of the thesis committee, and by Drs. Gutmann, Ledoux-Lebard, Garcia-Calderon and other members of the Faculté de médecine de Paris. The term "cancer ulcériforme" is applied to that type of primary gastric cancer which has the anatomic, radiologic and symptomatic characteristics in whole or large part of chronic benign gastric ulcer. The author properly distinguishes clinically between cancer ulcériforme, ulcère transforme and cancer ulcère.

The author is in almost entire agreement with the point of view of many other investigators who maintain that gastric cancer in its circumscribed, ulcerating, non-neoplastic form may masquerade readily as benign ulcer and that differentiation may be impossible short of performing histologic examination of the resected specimen. The danger of relying on impressions derived from macroscopic examination of a specimen at the time of operation as the basis for advising a conservative surgical procedure is emphasized. However, disappearance of the niche following treatment for ulcer and disappearance of the clinical signs are extremely reassuring. Of the laboratory methods available, search for occult hemorrhage at varying intervals of time appears to be the most reliable. The author also feels that the most important factor in making the diagnosis of ulceriform cancer is the roentgenologic examination. Of the niches which, when observed, arouse suspicion of the presence of carcinoma, the niche termed "en plateau," the triangular niche and the niche termed "encastrée" are the most characteristic. The meniscus sign, l'image en pessaire, stressed by German and American authorities, is described last. In the judgment of the author the large size of the niche, the irregularity of its contour and the discontinuation of the folds are important signs but are not pathognomonic.

Contrary to the opinion of some writers at home and abroad, the absence of tenderness on palpation of the niche has no differential diagnostic value according to the author. Situation of the niche on the greater curvature of the stomach or on the walls of the stomach does not signify the presence of cancer necessarily. He has observed that, whereas ulcer niches have a marked tendency to become smaller and to disappear following ulcer therapy, carcinomatous niches persist and increase in size. This increase in the size of the niche, even when accompanied by disappearance of symptoms, justifies performance of radical resection.

Although the bibliography consists largely of reference to French literature, the more important American, English and German contributions are included.

Developmental Abnormalities of the Eye. By Ida Mann, D.Sc., M.B., B.S., Surgeon Royal London Ophthalmic (Moorfields) Hospital. With a foreword by Sir John Herbert Parsons, C.B.E., D.Sc., LL.D. Published for the British Journal of Ophthalmology. Cloth. Price, $15. Pp. 444, with 284 illustrations. New York: Macmillan Company; Cambridge: University Press, 1937.

Any attempt to deal intelligently with developmental abnormalities of the eye must fall of its own weight unless supported by comprehensive knowledge of the embryology of the human eye and of animal eyes, as well as by a wide clinical experience from which a great deal of information concerning pathologic conditions of the eye has been gathered at first hand. The author of this book is peculiarly fitted by her extensive studies in embryology and comparative anatomy, and by a wide clinical experience, to correlate abnormalities of the eye that may seem to be pathologic, in the sense that they are the sequelae of disease, with the development of that organ under influences that are normal or abnormal. The method of approach to the subject that is of importance to a clinician is a logical exposition of the sequence of events during the stages of early development of the eye with the injection of hypothetical cases of abnormalities that may be expected if certain things happen at certain stages of embryonic growth.

The first chapters are devoted to a discussion of the mechanism of the production of developmental abnormalities as revealed by study of teratology and fetal pathology. Sufficient reference to experimental work bearing on the subject is included in the text to remind the reader of forgotten hours spent in poring over dry anatomic treatises and to revive an interest in the academic foundation of his clinical practice which may now seem so remote and so obscure. The problem of genetics, "possibly the most important of all, in their relation to anomalies," is illustrated on the basis of experimental investigation on the fruit fly, of which all ophthalmologists have some knowledge. "After birth, diseases and environmental changes are no longer classified among the causes of developmental anomalies, and such anomalies as arise during the early years are germinal or mutational in origin. Examples of such conditions are medullation of the retinal nerve fibers and heterochromia."

There are 418 pages of clearly written text, amply illustrated by schematic drawings, photomicrographs and many colored plates. The chapters on abnormalities of the fundus oculi explain ophthalmoscopic appearances of the disk, choroid and retina that may represent variations, deviations or arrests in embryologic development and the stage of development at which the incident probably occurred. Familial and hereditary degeneration, such as retinitis pigmentosa, the Lawrence-Moon-Biedl syndrome, dystrophies, vascular anomalies and von Hippel-

Lindau's disease, are considered from the standpoint of the influences that brought them about and why the abnormal development continues after birth. Most interesting are the sections devoted to abnormalities of the iris, lens and cornea. Distinction between developmental and acquired anomalies of these structures is not always easy, but many of the difficulties are explained by natural processes which the author points out.

For the student of anatomy the book brings to attention the observations of clinical practice that are so essential to understanding the significance of abnormal conditions of growth and development, either in natural or in experimental environment, and to the practitioner of ophthalmology it makes available the results of years of careful clinical observations by distinguished physicians and the patient researches of students working in the laboratories of the fundamental sciences.

Die Störungen der Sexualfunktion bei Mann und Weib. Von Dr. Ludwig Chiavacci. Mit einem Geleitwort von Prof. Dr. Otto Pötzl. Paper. Price, 4.60 marks. Pp. 147. Leipzig & Vienna: Franz Deuticke, 1938.

The title of this small monograph, which presupposes a discussion of the disorders of the sexual function, is really misleading. The main portion of the work is taken up with impotence and only about fifteen pages is reserved for sterility. The subjects of masturbation, pollution, priapism, satyriasis, nymphomania, vaginismus and similar definite disorders of the sexual function in both sexes are not considered at all. There are, however, some sensible views uttered in the text. The author states correctly that impotence and frigidity are not diagnoses but symptom complexes and that for this reason the treatment varies with the individual cause. This is a sensible and necessary conception, because of late many drugs and operations have been recommended for impotence without any attempt at differentiating with regard to the basic pathologic condition.

The author warns against considering every form of impotence as imagination on the part of the patient and against neglecting to consider organic conditions in relation to impotence or to consider everything about impotence as psychic. In such a small monograph, too much space is wasted on the consideration of all the possible causes of impotence, many of which are factors only in rare cases. The author bemoans the fact that our civilization has a tendency to thwart natural potency and so make for impotence, since both the male and the female cannot indulge in coitus just when they most desire it but must restrain themselves on account of decency and other considerations till they find a proper time and place. This restraint, according to the author, works against natural coitus. However, he ignores the fact that after centuries of civilization the normal adult of both sexes has become accustomed to such restraint without any hardship and is therefore different from the brute animal. Were it otherwise, all men would be sufferers from satyriasis and become rapists.

Although pathologic conditions in the posterior urethra are mentioned as a possible cause of rapid and premature ejaculation, the author seems to doubt their relationship. He wisely decries the tendency to recommend certain articles of diet which the general public and some physicians believe are advantageous for potency. It is positively harmful to recommend, as the author does in those cases in which the impotence in the husband is supposed to be due to a sexual inadequacy or frigidity on the part of the wife or partner, a change of the sexual partner. Of course he says that this advice should be given only on the rarest occasions, but one can easily see to what latitude such advice can be stretched by one who only awaits an excuse for infidelity. He advises that the physician should not directly recommend this procedure but should explain the situation plainly to the husband on the ground that the latter will generally understand and take the hint. Such an underhand method of procedure is beneath the dignity of the medical profession, to say the least.

The author has some sensible views as to the uselessness of various forms of baths, diathermy and similar modalities in the therapy of most forms of impotence. His treatment of impotence is largely a naming of the various patented endocrine preparations and he especially prefers the pluriglandular preparations, the very ones which endocrinologists in America decry as essentially unscientific. Hardly any mention is made of prostatic treatment and the treatment of the prostatic urethra with silver nitrate instillations, except the occasional mention of a cold sound.

His discussion of sterility in both sexes might serve a student who is preparing himself for an examination on this subject, but it is really of little practical use either to the general practitioner or to the specialist. The entire subject is covered in fifteen pages and the diagnosis takes only about one and a half pages. The treatment is considered in about five pages and is virtually an enumeration of the various forms of treatment employed in this condition. Neither the Rubin nor the Huhner test is mentioned and these names do not appear in the author's bibliography.

Medical Records in the Hospital. By Malcolm T. MacEachern, M.D., C.M., D.Sc., Associate Director, American College of Surgeons. Cloth. Price, $3. Pp. 374, with 134 illustrations. Chicago: Physicians' Record Company, 1937.

From the experienced author of "Hospital Organization and Management" has come a new volume, equally authoritative and practical, covering every phase of the medical record work in hospitals. A veritable storehouse of information, this book represents a compilation of earlier writings modified in the light of present day experiences and supplemented by data on the new developments in the record field. In logical order the material is presented in nine chapters dealing with the development of the medical record, record librarian, contents and forms, methods of securing the medical record, supplementary records in adjunct departments, preservation of the medical record, uses, clinical photography and the hospital medical library. Interspersed are approved forms for every part of the clinical and statistical records and other valuable illustrations and charts. Five of the chapters contain addenda presenting curriculums on the hospital and college training of record librarians, regulations governing the registration of record personnel, history outlines, sample case records, specialty forms, palm prints and footprints in the identification of the new-born, regulations concerning the legal use of records and transcripts, records of staff meetings and lists of textbooks, periodicals and publishers. There is an extensive bibliography, a list of illustrations and forms and an ample index of fourteen pages.

This comprehensive book, written in a masterly and systematic manner, is a complete answer to the record problems of today. It has introduced many new subjects of increasing importance to the record personnel and has helped greatly to elevate the status of the record department. There are timely discussions on the record difficulties in small hospitals, classification of major and minor operations, frequency of progress records and the need for condensed nurses' bedside notes in order to conserve time and paper and eliminate the bulk of irrelevant material which only creates a difficult filing problem.

This volume is particularly valuable to the record personnel as a textbook and guide but should prove equally useful to hospital administrators, staff physicians, the record committee, department heads, resident physicians, interns, nurses, social service workers and technical personnel participating in the care of patients.

Occidental Therapeutics in the Netherlands East Indies During Three Centuries of Netherlands Settlement. (1600-1900). By Dr. D. Schoute. Cloth. Pp. 214, with 4 illustrations. Batavia: Netherlands Indies Public Health Service, 1937.

"The purpose of this publication," says the author, "is to supply a concise summary, in a universal language, of the researches carried out by him with the consent of the Indian government on the development of the medical service in the Netherlands East Indies. In these years of widespread political tension, each colonizing country will have to ask itself how it has acquitted itself of its task and whether it has, apart from obtaining advantages for itself, also brought welfare and real prosperity to the lands over which it holds sway." He quotes Field Marshal Lyautey to the effect that the only excuse for colonization is medicine, and while the author does not go as far as this, preferring to include in that excuse other contributions to the happiness of the inhabitants of the colonies, a great and valuable part of it must be allotted to medical science. The body of this book makes almost as fascinating reading as do the stories of early exploration, for it starts with the beginning of Netherlands colonization enterprise under the United

110
938

Netherlands East India Company. It describes the kind of ships that the company sent out and their meager medical equipment. The care of the health of the employees of the company was entrusted to "surgeons," that is, members of the barbers' guild, whose examination consisted in the grinding of three crude pieces of iron into bleeding scalpels and the performing of some bleedings on test persons. He defends this condition by pointing out that the company would have been unable to supply the large number of academically trained physicians required and also that the knowledge of the physicians of those days would probably have been no more efficient against the murderous diseases that ravaged the ships and the colony because of the state of ignorance that existed. No wonder that nearly 8 per cent of all who started out on a voyage to the colony were reported lost. After the establishment of Batavia a hospital was founded and in the course of time hospitals were established elsewhere, but throughout the 200 years of the existence of the Netherlands East India Company the medical service was exclusively for the benefit of the employees of the company. Among the general population the mortality from endemic as well as epidemic diseases was very high. Military medical service that next continued the work of the East India Company extended itself also in the direction of general sanitation and this, together with the advances in medical science that occurred most especially during the last century, has greatly improved both the mortality and the morbidity conditions. Dr. Schoute's book must be accepted as an interesting and important contribution to the history of medicine in the colonies of European nations.

An Introduction to Nematology. By B. G. Chitwood and M. B. Chitwood. Section I, Part 1. Paper. Pp. 53, with 53 illustrations. Baltimore: Monumental Printing Company, 1937.

This is the first number of a projected treatise from the zoological point of view in the much neglected field of nematology. The nematode worms from an ecological and medical point of view are of great importance. They abound in the soil and in organic wastes of civilization, and in humus, sewage, sludges, and offal of organic origin. They infest important cultivated plants such as beets, parsnips, onions, potatoes, sugar cane, pineapples and wheat. They invade gardens, dwarf chrysanthemums and daffodils and make greenhouse soils unproductive. They occur as parasites in the bodies of most animals, and scores of different species parasitize the organs and tissues of man. Although they are relatively simple in structure, this very simplicity makes their classification and identification difficult and uncertain. What they lack in structural complexity they more than make up in diversity in life cycles and in facultative abilities in surviving in other hosts than those in which they normally occur. Furthermore, some of their ova at least have astounding powers of survival under adverse conditions of environment. The Chitwoods plan a work in ten numbers, with specialists as collaborators, in which an accurate and comprehensive account of this difficult group of organisms will be given. If the high standard of the first number is maintained in later ones, the completed work will be an invaluable aid to perplexed parasitologists as well as to physicians, veterinarians and investigators of soil science. The authors, as members of the staff of the United States Department of Agriculture, have library facilities, collections, connections and associates which, it is to be hoped, will make possible the early completion of this much needed work.

Report of the Eighth Australian Cancer Conference Held at Canberra, 13th-16th April, 1937. Commonwealth of Australia. Paper. Pp. 66. Canberra: L. F. Johnston, 1937.

This is a report of the efforts of the Australian government and of the individual Australian states to educate the public in the importance of early diagnosis and also to train the physician in the methods of treating neoplasms, especially in the use of radium, in which the commonwealth has staged an interesting experiment. Ten Gm. of radium has been purchased and radon is sent throughout the country to qualified physicians, the use of the element itself being restricted to a few large hospitals. Tables of deaths from malignant disease from 1908 to 1935 are given, showing that the recorded death rate has nearly doubled in this period and, in addition, analyses of the different types of neoplasms showing, for example, that cancer of the tongue is some twenty times more frequent in males than in females. There are also tables showing the extraordinary frequency of cancer of the skin in Australia, a fact which has been used to buttress the idea that sunlight is a causative agent in this type of cancer. Another section comprises short reports of investigations on the measurement of x-rays and radium, the biologic effects of radiation, possible developments of radiation therapy in the future, some general cancer research, and a convenient classification of tumors for use in reporting deaths from cancer. The pamphlet is interesting not so much for the facts which it contains as for the picture it gives of an attempt to develop by government initiative in a relatively homogeneous community with widely distributed population centers an efficient use of various types of radiation in the treatment of cancer.

Let's Help the Doctor. By Margaret O'Donovan-Rossa, R.N. Cloth. Price, $1.50. Pp. 141, New York: Devin-Adair Company, 1937.

This book may not be the worst of books on home nursing, but it is not even moderately good. It would have been better if the author had adhered to her announced intention, as expressed in the introduction, of describing simple home nursing procedures. Instead, she puts in a chapter on vitamins, which is not only out of place but entirely inadequate and shows several evidences of poor judgment with respect to what every mother ought to know about vitamins as, for example, "How can I recognize body symptoms which will tell me if my family is getting enough, too much or too little of each of the vitamins?" Such advice contributes to the prevalence of the great American disease vitamin-jitters, which has attained the magnitude of an epidemic. The introduction of poetry or, at any rate, verse, into the text is unusual in this type of writing and seems like a forced attempt to be sprightly, as do a number of other inappropriate interpolations. The chapter on the symptoms of diseases is not only out of place but is poorly prepared, conducive to home diagnosis of serious disease and potentially dangerous. The "simple care of pregnancy," including illegal operations (!), in six short pages, is altogether too simple. The facts of life, in four pages, are simpler still—including the menopause, menstruation and what a young girl ought to do when "alone with a young man." The chapter on first aid is full of slipshod and poorly selected information and bad advice. Much of the material appears to have been assimilated none too well from medical digests of the "compend" type to which medical students resort in the last hours before final examinations. The best recommendation is "Let's Help the Doctor" by not reading this book.

Keeping Well. The Second Series of Radio Talks Broadcast Every Tuesday by the Baltimore City Health Department and the Medical and Chirurgical Faculty of Maryland, November 21, 1933-April 21, 1936. Paper. Pp. 284, with one illustration. Baltimore: Baltimore City Health Department, Bureau of Health Information, [n. d.].

This collection of radio talks is of exceptional merit. In their original mimeographed form they have been received weekly by the American Medical Association Bureau of Health and Public Instruction, and through the courtesy of the Baltimore Health Department and the Medical and Chirurgical Faculty of Maryland many of them have been added to the Bureau's radio library and have been broadcast again by medical societies in many parts of the country. This appearance now in a paper-bound volume brings them together in handy form, constituting not only an interesting record of a valuable service in health education by radio but a convenient book of briefs, in language for the lay reader or listener, of almost 150 popular and timely health topics. Such a book should be in the libraries of health departments and county medical societies sponsoring speakers' bureaus and radio programs, as convenient and authentic quick reference material and suggestions for topics and for the successful handling of them.

In the Lives of Men. By Alan Hart. Cloth. Price, $2.50. Pp. 451. New York: W. W. Norton & Company, Inc., 1937.

This novel with a medical background is another of the contributions of Alan Hart. These medical novels are of interest but apparently not of sufficient appeal to attract a wide audience. Because of their locale (in the Northwest) they should appeal particularly to the physicians of that area.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Medical Practice Acts: Removal of Hair by Electrolysis Not the Practice of Medicine.—In the opinion of the supreme court, appellate division, first department, New York, the removal of hair from the human face by an operator of a beauty parlor by electrolysis does not constitute the practice of medicine within the meaning of the medical practice act of New York. Superfluous hair neither constitutes a "disease," "deformity" nor "physical condition" within the meaning of the act. In reaching this conclusion the court quoted as follows from the dissenting opinion in *Engel* v. *Gerstenfeld*, 168 N. Y: S. 434 (reversed in 171 N. Y. S. 1084):

> Concededly there is nothing in the record to show that the growth of hair on a woman's face is a disease. The question then arises: Was it a "deformity" within the meaning of the statute? The Century Dictionary describes a "deformity" as a "deformed or misshapen condition; an unnatural growth, or a distorted or misshapen part or member; disfigurement; as a bodily deformity." The statute does not state or contain a definition of any of these words. The presumption, therefore, is that they were used in their ordinary sense, and with their ordinary intent. A growth of hair on a woman's face can certainly not be a "deformed or misshapen condition." In considering the second meaning given, viz., "an unnatural growth or a distorted or misshapen part or member," the words "unnatural growth" cannot but pertain to matters that are ejusdem generis, when joined with the expression "or a distorted or misshapen part or member" common sense dictating to us that in the ordinary acceptation of such terms reference must naturally be to a physical growth or deformity, such as a web foot or a hunch back. Proceeding to the third meaning given by the Century Dictionary, we find that the word "disfigurement" is stated to be "the state of being disfigured," i. e., "physically marred in any manner." It would clearly be absurd for us to say that "physically marred" would be applicable to the case at bar.
>
> . . . Was this a "physical condition" within the meaning of the statute? A physical condition is, I take it, any condition that is perceptible by the senses. Therefore, a physical condition is anything or any condition about the body which is the subject of observation. It could very forcibly be argued that the growth of a finger nail, or premature baldness, or a visible birthmark, or any growth upon the body is a physical condition, but the legislature, I am sure, did not intend that such an interpretation should be put upon these words. It is quite as logical to say that a manicurist or a barber is guilty of practicing medicine without a license in removing parts of the finger nail or the hairs on a man's face, as this plaintiff is in removing hair from a woman's face.

The present case was a test case and the court was convinced that the medical practice act was never intended to cover the type of beauty culture here involved. The judgment of conviction was therefore reversed.—*People v. Lehrman (N. Y.), 296 N. Y. S. 580.*

Malpractice: Mistaken Diagnosis by Chiropractor; Testimony of Doctor of Medicine Admissible.—The plaintiff, while carrying a heavy timber, accidentally fell and injured his hip. The defendant, a chiropractor, attended him. Alleging that the defendant improperly diagnosed his condition and failed carefully and skilfully to treat him, the plaintiff sued the defendant. The trial court gave judgment for the plaintiff, and the defendant appealed to the Supreme Court of Utah.

The defendant, according to the complaint, informed the plaintiff that the pain he was suffering in his hip was rheumatism, for which he adjusted the plaintiff's spine over a period of approximately eight months. It subsequently developed that the plaintiff was suffering from osteomyelitis of the hip. Much suffering was alleged to have been endured because of the defendant's negligent treatment of the condition. On appeal, the defendant contended, among other things, that the trial court erred in permitting witnesses who were licensed to practice medicine and surgery to testify, urging that the only evidence that was admissible bearing on his malpractice was the testimony of chiropractors. With this contention the Supreme Court disagreed. In states, the court said, where the different schools of healing are classified into allopathic, homeopathic, osteopathic, chiropractic or other schools there is ample authority to support the contention that the professional conduct and treatment of a practitioner of one particular school should be tested by the rules of his school and not by those of other schools. In Utah, however, chiropractors obtain licenses under a provision of the medical practice act authorizing the issuance of licenses "to practice the treatment of human ailments without the use of drugs or medicine and without operative surgery in accordance with the tenets of the professional school, college or institution of which the applicant is a graduate as designated in his application for license." An applicant for such a license is required to take an examination of the same character as that required of an applicant for a license to practice medicine and surgery in all branches, excepting materia medica, therapeutics, surgery, obstetrics and theory and practice. Thus, the court pointed out, a person who has a license and holds himself out as a chiropractor holds himself out as qualified to treat human ailments with all the qualifications of one holding a license to practice medicine in all its branches, "excepting therefrom materia medica, therapeutics, surgery, obstetrics and theory and practice." The legislature intended that a license to practice medicine and surgery should cover the whole field of treatment of human ailments. Such a practitioner, therefore, possesses the qualifications to testify as an expert in a malpractice case charging malpractice in diagnosis or negligent treatment of human ailments. The trial court did not err in admitting the testimony of the doctors of medicine.

The fact that the treatment given by the defendant, said the court, did not effect a cure could not constitute the basis of a cause of action. Neither does the fact that a practitioner fails to diagnose or treat a patient in the same way as another practitioner constitute malpractice. Whether a person coming from a school of chiropractic training should be required to have a knowledge of the subjects required of a practitioner of medicine and surgery in all branches, except those subjects specified, is not for the court to determine. The law was passed, not for the purpose of imposing burdens on those desiring to qualify to treat human ailments, but to protect the public. The court may not concern itself with respect to the policy of a law; that is exclusively a legislative function.

The court finding no error in the proceedings of the trial court, the judgment in favor of the plaintiff was affirmed.—*Walkenhorst v. Kesler (Utah), 67 P. (2d) 654.*

Malpractice: Statute of Limitations in Relation to Bill of Particulars Setting Forth New Cause of Action.—From July to December 1929 the plaintiff underwent a course of treatment from the defendant, a physician, for hemorrhoids, during which time a hemorrhoidectomy was performed. The following May the patient suffered from a severe proctitis with a spasm of the sphincter muscle. The defendant again attended him, relaxed the sphincter ani under a general anesthetic, and instructed him to return several days later. On the latter date no treatment was administered because the patient "was suffering from a sore throat and not feeling well." The patient then consulted another physician. Eventually a streptococcic infection set in, resulting in a pelvic abscess. On May 11, 1932, the patient sued the defendant for damages for malpractice. The trial court gave judgment for the plaintiff, and the defendant appealed to the Supreme Court of Michigan.

The plaintiff's declaration alleged that on May 12, 1930, the defendant was employed to perform a hemorrhoidectomy on him and that owing to the negligent performance of that operation a streptococcic infection set in, resulting in a pelvic abscess. To this declaration the defendant filed an answer alleging that any treatment administered to the plaintiff by the defendant terminated on Dec. 7, 1929, and as to this course of treatment the two years statute of limitations was pleaded. When the case came to trial, in April 1934, the plaintiff was permitted to file a bill of particulars specifying the negligent acts relied on, which stated that the negligence, unskilfulness and malpractice of the defendant consisted in not properly diagnosing the patient's condition on May 12, 1930, and in relaxing the sphincter muscle in the presence of the existing proctitis. To this bill of particulars the defendant objected, claiming that it set out a cause of action not stated in the declaration and that the cause of action thus set out was also barred by the statute of limitations. The undisputed testimony, the court said, was that the hemorrhoidectomy was performed prior to December 1929, and since the declaration alleged negligence in connection with

110
938

that operation the action was barred by the statute of limitations. The bill of particulars filed in April 1934, continued the court, alleged malpractice in connection with the relaxing of the sphincter muscle, May 12, 1930. It abandoned the claim of malpractice in connection with the hemorrhoidectomy and thus alleged a new cause of action not contained in the original declaration. "It is not within the discretion of a trial court to permit an amendment which states a cause of action barred by the statute of limitations."—*Bockoff* v. *Curtis*, 241 Mich. 553, 217 N. W. 750. The Supreme Court therefore reversed the judgment of the lower court.—*O'Rourke v. Deffenbaugh (Mich.), 273 N. W. 749.*

Society Proceedings

COMING MEETINGS

Alabama, Medical Association of the State of, Mobile, Apr. 19-21. Dr. D. L. Cannon, 519 Dexter Ave., Montgomery, Secretary.

American Association for Thoracic Surgery, Atlanta, Ga., Apr. 4-6. Dr. Richard H. Meade Jr., 2116 Pine St., Philadelphia, Secretary.

American Association of Anatomists, Pittsburgh, Apr. 14-16. Dr. George W. Corner, 260 Crittenden Blvd., Rochester, N. Y., Secretary.

American Association of Genito-Urinary Surgeons, Atlantic City, N. J., May 2-4. Dr. Henry L. Sanford, 1621 Euclid Ave., Cleveland, Secretary.

American Association of Pathologists and Bacteriologists, Atlantic City, N. J., May 3-4. Dr. Howard T. Karsner, 2085 Adelbert Road, Cleveland, Secretary.

American Association of the History of Medicine, Atlantic City, N. J., May 2. Dr. E. J. G. Beardsley, 1919 Spruce St., Philadelphia, Secretary.

American Association on Mental Deficiency, Richmond, Va., Apr. 20-23. Dr. E. Arthur Whitney, Washington Road, Elwyn, Pa., Secretary.

American Bronchoscopic Society, Atlantic City, N. J., Apr. 30. Dr. Lyman Richards, 319 Longwood Ave., Boston, Secretary.

American College of Physicians, New York, Apr. 4-8. Mr. E. R. Loveland, 4200 Pine St., Philadelphia, Executive Secretary.

American Gastro-Enterological Association, Atlantic City, N. J., May 2-3. Dr. Russell S. Boles, 1901 Walnut St., Philadelphia, Secretary.

American Laryngological Association, Atlantic City, N. J., May 2-4. Dr. James A. Babbitt, 1912 Spruce St., Philadelphia, Secretary.

American Laryngological, Rhinological and Otological Society, Atlantic City, N. J., Apr. 27-29. Dr. C. Stewart Nash, 277 Alexander St., Rochester, N. Y., Secretary.

American Neurological Association, Atlantic City, N. J., May 2-6. Dr. Henry A. Riley, 117 East 72d St., New York, Secretary.

American Orthopedic Association, Atlantic City, N. J., May 3-5. Dr. Ralph K. Ghormley, 110 Second Ave. S.W., Rochester, Minn., Secretary.

American Physiological Society, Baltimore, Mar. 30-Apr. 2. Dr. A. C. Ivy, 303 East Chicago Ave., Chicago, Secretary.

American Society for Clinical Investigation, Atlantic City, N. J., May 2. Dr. J. M. Hayman Jr., 2065 Adelbert Road, Cleveland, Secretary.

American Society for Experimental Pathology, Baltimore, Mar. 30-Apr. 2. Dr. Paul R. Cannon, University of Chicago, Chicago, Secretary.

American Society for Pharmacology and Experimental Therapeutics, Baltimore, Mar. 30-Apr. 2. Dr. G. Philip Grabfield, 319 Longwood Ave., Boston, Secretary.

American Society of Biological Chemists, Baltimore, Mar. 30-Apr. 2. Dr. H. A. Mattill, Chemistry Bldg., State University of Iowa, Iowa City, Secretary.

American Surgical Association, Atlantic City, N. J., May 2-4. Dr. Charles G. Mixter, 319 Longwood Ave., Boston, Secretary.

American Therapeutic Society, New York, Apr. 1-2. Dr. Oscar B. Hunter, 1835 Eye St. N.W., Washington, D. C., Secretary.

Arizona State Medical Association, Tucson, Apr. 21-23. Dr. D. F. Hardigan, 15 East Monroe St., Phoenix, Secretary.

Arkansas Medical Society, Texarkana, Apr. 18-20. Dr. W. R. Brooksher, 602 Garrison Ave., Ft. Smith, Secretary.

Association of American Physicians, Atlantic City, N. J., May 3-5. Dr. Hugh J. Morgan, Vanderbilt University Hospital, Nashville, Tenn., Secretary.

Congress of American Physicians and Surgeons, Atlantic City, N. J., May 3-4. Dr. John T. King Jr., 1210 Eutaw Place, Baltimore, Secretary.

District of Columbia, Medical Society of the, Washington, May 4-5. Dr. C. B. Conklin, 1718 M St. N.W., Washington, Secretary.

Federation of American Societies for Experimental Biology, Baltimore, March 30-April 2. Dr. D. R. Hooker, 19 West Chase St., Baltimore, Secretary.

Georgia, Medical Association of, Augusta, Apr. 26-29. Dr. Edgar D. Shanks, 478 Peachtree St. N.E., Atlanta, Secretary.

Louisiana State Medical Society, New Orleans, May 2-4. Dr. P. T. Talbot, 1430 Tulane Ave., New Orleans, Secretary.

Maryland, Medical and Chirurgical Faculty of, Baltimore, Apr. 26-27. Dr. Walter Dent Wise, 1211 Cathedral St., Baltimore, Secretary.

Mississippi State Medical Association, Jackson, Apr. 19-21. Dr. T. M. Dye, McWilliams Bldg., Clarksdale, Secretary.

Missouri State Medical Association, Jefferson City, May 2-4. Dr. E. J. Goodwin, 634 N. Grand Blvd., St. Louis, Secretary.

Nebraska State Medical Association, Lincoln, Apr. 26-28. Dr. R. B. Adams, Center-McKinley Bldg., Lincoln, Secretary.

North Carolina, Medical Society of the State of, Pinehurst, May 2-4. Dr. T. W. M. Long, Roanoke Rapids, Secretary.

Philippine Islands Medical Association, Zamboanga City, Apr. 19-22. Dr. A. S. Fernando, 837 Taft Ave., Manila, Secretary.

Tennessee State Medical Association, Nashville, Apr. 12-14. Dr. H. H. Shoulders, 706 Church St., Nashville, Secretary.

CENTRAL SOCIETY FOR CLINICAL RESEARCH

Tenth Annual Meeting, Held in Chicago, Nov. 5 and 6, 1937

The President, DR. DAVID P. BARR, St. Louis, in the Chair

(Continued from page 768)

Extrarenal Uremia

DRS. F. H. SCHARLES and ABRAHAM SOPHIAN, Kansas City, Mo.: The nonprotein nitrogen fraction of the blood can become elevated in conditions other than those affecting the kidney directly, particularly when there is upset of the fluid and inorganic salt balance. It is our purpose in this paper to focus attention on this so-called extrarenal uremia, by presenting three illustrative cases with their clinical manifestations and the laboratory and renal function studies. The first case is one associated with severe diarrhea; the second patient had intractable vomiting after an alcoholic debauch; the third patient used large doses of alkali with resultant alkalosis and elevated nonprotein nitrogen. These returned to normal following the administration of fluids and restoration of the salt balance.

DISCUSSION

DR. GEORGE B. EUSTERMAN, Rochester, Minn.: There are a number of extrarenal causes for uremia. In addition to those cited, one should also mention severe gastro-enteric hemorrhage, protracted vomiting either functional or organic, crises occurring during Addison's disease, and so on. I agree that dehydration, and loss of electrolytes as evidenced by hypochloremia, rather than primary renal injury, are the important underlying factors. The mechanism underlying uremia following hemorrhage apparently is a combination of absorption of blood from the bowel, and transient renal dysfunction, the result of acute anemia. Disease of the kidneys, liver and adrenals greatly enhances disturbances of acid-base equilibrium following the administration of basic and acid salts. Excess administration of salt and fluid causes severe edema of the tissues, especially disadvantageous in cases in which operation is contemplated.

DR. W. S. HOFFMAN, Chicago: Two laboratory procedures that aid in the diagnosis of these extrarenal "uremias" should be mentioned. If the specific gravity of the urine is found to be about 1.030, due allowance being made for albumin, it is very likely that the kidney function is normal and that the nitrogenous retention is due to lack of sufficient fluid to produce an adequate amount of urine. The second procedure is not so simple but is more exact: the determination of the serum total base concentration. Values below 150 milliequivalents per liter indicate not only dehydration but also that the loss of sodium has surpassed the loss of water and that the remaining extracellular fluids of the body are hypotonic. Unfortunately, most methods for estimating total base are too difficult and too tedious to be of routine use. As Peters and Van Slyke have pointed out, some idea of the value of the total base concentration can be obtained by adding the chloride and bicarbonate concentrations. In the last few years, too, methods for serum sodium have been made simpler and should soon be available for clinical laboratories.

DR. HUGO A. FREUND, Detroit: In certain cases of intracranial tumor, high nitrogen levels are encountered. They are not to be explained on the basis of electrolytic change. In Warthin's festschrift I reported a case in which high nitrogen levels obtained for a long time; when this patient died after operation for brain tumor, normal kidneys were encountered. As an example of the loss of electrolytic fluids, those of us who have seen mushroom poisoning (Amanita phalloides) noted that nonprotein nitrogen rises as high as 250, subsiding shortly after the acute symptoms have passed.

DR. F. H. SCHARLES, Kansas City, Mo.: The alkalinity that is usually present in these cases of lost electrolytes and elevated nonprotein nitrogen is most probably a compensatory affair, an attempt of the body to keep the equilibrium of the system. That has been conclusively shown by Peters. The first loss of electrolytes is chloride with a compensatory rise in the bicarbonate.

Sodium Chloride Tolerance in Chronic Nephritis: Potassium and Sulfate Ions

DR. M. HERBERT BARKER, Chicago: When sodium chloride was added to the basal constant sodium-potassium-chloride-nitrogen-sulfur diet in severe cases of chronic glomerular nephritis a rapid rise in blood pressure and a sharp fall in urea clearance were noted. The effect of sodium bicarbonate was somewhat less, but in both cases the addition of ammonium sulfate was associated with a decrease of the blood pressure and an arrest of the falling urea clearance. Substitution of potassium chloride and potassium citrate equal to the amounts of sodium chloride and sodium citrate was attended by an improvement of urea clearance, and a diuresis usually occurred when there was edema. These observations suggest a great intolerance of sodium salts and the beneficial effects of potassium and sulfate ions in the maintenance of the person with a severely damaged kidney.

DISCUSSION

DR. W. E. POST, Chicago: Sodium salts in large amounts may be dangerous even to the normal patient, and Dr. Eusterman has called attention to this critical stage of the administration of salts or alkalis on account of the appearance of edema. In cases in which there is danger of the salt passing into the general body tissues it has seemed to me especially dangerous. Dr. W. S. Hoffman and I did some work about four years ago on edema and found that we could force the sodium out of the tissues by giving low sodium diet and plenty of water. Nephrotic edema disappears quite rapidly in cases of nephrosis. In cases in which there is danger of the tissues holding the sodium, as in infection or some intoxication, the edema increases rapidly. It emphasizes the necessity for taking into consideration the pathologic processes going on in the body, such as infection, and also that somewhat more care be taken in the administration of large quantities of salt.

DR. M. HERBERT BARKER, Chicago: Most of the patients of course had a high grade acidosis. Many of them experienced renal crises with the carbon dioxide falling rapidly. To add to that an acid salt, such as ammonium chloride, will kill the patient. I believe that the sodium injury is associated with sodium retention. Chlorides must not be pushed beyond the optimum normal. Ammonium nitrate is the safer salt to use when one is giving ammonium salts, because it is essentially a neutral diuretic. Dr. Post's remarks are timely. When many patients in the second half of life are subjected to surgical operation and receive only 3 to 8 liters of salt solution a day, or from 50 to 80 Gm. of salt, there is grave danger.

Lipoid Nephrosis

DRS. FRANCIS D. MURPHY, JOHN GRILL, EDWARD R. ANNIS and LOUIS M. WARFIELD, Milwaukee: The use of the term "lipoid nephrosis" to indicate a disease separate and distinct from chronic glomerulonephritis has been criticized by some pathologists and clinicians alike. A clinical study of cases over a prolonged period may help to clarify some of the disputed points in connection with the question of the identity of lipoid nephrosis. Nine cases are described which fulfilled the rigid requirements for a diagnosis of lipoid nephrosis. Two of the patients died and were studied post mortem, one is under observation at the present time, and six recovered completely. Microscopic examinations of the kidneys failed to show typical evidence of chronic glomerulonephritis. The length of time these patients were studied varied from three months to fifteen years. Most of them were studied for more than seven years. This report tends to support the view that there is justification for the distinction between lipoid nephrosis and chronic glomerulonephritis. There is ample defense for this on the grounds of the good prognosis of lipoid nephrosis as contrasted to the poorer one in chronic glomerulonephritis. Recently reports by some well known pathologists indicate that lipoid nephrosis is not an atypical form of glomerulonephritis. Our pathologic studies are given, and, although they are too meager from which to draw final conclusions, they support the view that in lipoid nephrosis evidence of chronic nephritis is lacking.

DISCUSSION

DR. WILLIAM A. THOMAS, Chicago: I believe that pure lipoid nephrosis is a degenerative process which occurs most frequently in connection with other degenerative processes, such as infection and certain types of Bright's disease. In the last five years Dr. Post and I have made a study of the toxemias of pregnancy at Presbyterian Hospital. All the patients in the antepartum clinic who showed disturbances came into the hospital. There were many cases of albuminuria and edema which turned out to be cases of nephrosis. They are not cases of toxemia of pregnancy. They are induced by the extra load of pregnancy and many clear up during pregnancy. They fulfil all the requirements of lipoid nephrosis. Some have been followed three or four years, some with recurrence and some without recurrence. We have felt that entirely aside from the toxemia of pregnancy many are pure cases of lipoid nephrosis. Many attacks are precipitated by a severe chill. The edema subsides while the blood proteins are far below the limits of normal. In one case that Dr. Post and I recorded 55 pounds (25 Kg.) of water was lost in fifteen days, while the total serum proteins were 1.1 + and the serum albumin 0.67 Gm. I have seen complete recovery from edema while the serum albumin would drop below 2 Gm. in the blood.

DR. LOUIS LEITER, Chicago: At present there is no longer the problem of whether nephrosis is a metabolic or a renal disease. It is apparently renal. Although the tubular changes may be striking, it is pretty well established that nephrosis is a glomerular disease primarily; whether degenerative or inflammatory is beside the point. The real criterion in the differential diagnosis would seem to be the duration of the active disease. It is one thing to examine the patient many years after the symptoms have disappeared and to find that the disease has not recurred, but it is another thing to establish recovery in an individual who has had active symptoms for several years. The latter would be most unusual in glomerular nephritis, but unfortunately we do not yet know when the process becomes irreversible. Most of the cases in this series will fall within the doubtful category. It will be noted that patients are reported as having active symptoms for less than three years from the onset of the disease. It is not unusual to see a patient with glomerular nephritis recover after two years of active disease. The only absolute way of settling the diagnosis between mild glomerular nephritis and genuine glomerular nephrosis would be to make biopsies, either during the active stage or shortly after recovery. Pathologic reports of minor inflammatory lesions in the glomeruli at necropsy mean little, since some terminal infection often complicates the situation. Most of the evidence on the inflammatory or degenerative nature of the changes in the glomeruli in patients with so-called nephrosis has been based on necropsy material and loses considerable value for that reason. Bell has described subclinical glomerulitis in a large series of cases in which there were infections of one type or another.

DR. CLAYTON J. LUNDY, Chicago: How can the edema in the second case be accounted for? The lantern slide showed a high protein and high albumin fraction.

DR. EDWARD ANNIS, Milwaukee: It is true that the blood albumin in the last case was not greatly depressed, and there was no reversal of the albumin globulin ratio. Though we studied this case for some time the edema did not fluctuate. The answer to the question is that there is no exact parallelism between the lowering of the blood albumin and the onset and disappearance of the edema.

DR. W. E. POST, Chicago: It seems to me that Bright's disease can be divided into three phases and one of them is this phase, one the vascular and one the renal or glomerular phase. A pathologic agent such as infection may do damage which leads to any one of them or any two of them or all three of them. So far as I know there is no impairment of renal function that causes generalized edema such as occurs in nephrosis. Furthermore, when this general tissue damage exists there is a nephrosis, in my opinion the same process associated with kidney damage or glomerular inflammation, and it is called nephrotic edema or hemorrhagic Bright's disease or glomerular nephritis, but the kidney may escape damage. In the management, if there is infection still active and damage still going on in the tissues, it is very difficult to rid those tissues of edema. If there is no infection and damage has ceased in the tissues, and degeneration is still present and edema still present, then the patient will be soon rid of edema if put

110
938

on a low sodium diet and given plenty of water. It seems to me that these particular types of lipoid nephrosis are simply ones in which the damage is manifested only in the tissues of the body and are not due to a degenerative form of kidney damage with renal impairment.

Colloid Osmotic Pressure in Diseases of the Liver and Relation to Ascites

DRS. HUGH R. BUTT and ALBERT M. SNELL, and ANCEL KEYS, PH.D., Rochester, Minn.: Many investigators have noted alterations in the concentration of the serum proteins during the course of certain types of hepatic disease. This measurement usually is considered to represent an accurate estimate of the colloid osmotic pressure of the blood serum. In normal man the average size of the protein molecules is fairly constant and the colloid osmotic pressure is therefore fairly closely related to the total protein concentration. In pathologic conditions, however, this relation is often so gross as to be nearly useless for purposes of prediction. We have observed a group of patients with hepatic disease who had ascites and edema and a low colloid osmotic pressure even when the serum protein values were within normal limits. These data indicate that the colloid osmotic pressure measured in the laboratory provides a much better estimate of the effective colloid osmotic pressure in the individual than the measurements of serum proteins, even when the albumin and globulin ratio is also determined. The effect of intravenous administration of solution of acacia on the colloid osmotic pressure of these patients is apparently beneficial.

DISCUSSION

DR. ROBERT W. KEETON, Chicago: Was a normal osmotic pressure found in any patients with cirrhosis who had an associated ascites?

DR. A. S. ALVING, Chicago: There is good evidence that in certain diseases serum albumin and globulin are not of normal quality. The recent work of Hewitt, who has found a new albumin fraction in serum, as well as the studies of blood proteins in nephrosis by Goettsch and Reeves in New York, is at least suggestive that in some diseases there may be abnormal proteins present in the blood, and they may have an abnormal osmotic pressure. Have these authors found something of that sort? Has an attempt been made to measure the molecular size of the proteins?

DR. J. D. BOYD, Iowa City: A boy five years ago, at the age of 6½ years, had typical lipoid nephrosis. For relief of his edema he received several injections of acacia, followed by subsidence of the edema. Later, this course was repeated. The boy has returned to the clinic on numerous occasions since his first discharge from the hospital. Even though edema has not been regularly present, albuminuria of considerable degree has persisted. His serum protein value has remained low, with reversal of the albumin-globulin ratio. During this period he has developed enlargement of the liver and spleen, associated for a time with definite evidences of compensatory circulation. During the past few months hypertension has appeared. His serum protein levels do not rise; with transfusions they have fallen to values of less than 2 per cent. We feel that this boy's liver has been damaged through storage of acacia until it no longer is able to function normally, and have thought that his inability to maintain a higher level of serum protein may well depend on the lessened ability of the liver to synthesize protein normally. In view of this experience, we have decided that the use of acacia for prolonged therapy is contraindicated and that conclusions as to its ultimate action must be based on long term observations.

DR. GEORGE B. EUSTERMAN, Rochester, Minn.: The intravenous administration of acacia solution in advanced cases of cirrhosis with ascites which are refractive to the usual diuretic measures has been disappointing so far in a small group of cases that I have observed.

DR. W. B. COOKSEY, Detroit: May I ask Dr. Butt whether he has had any reactions following the use of acacia? I recently asked Dr. Walter Cannon, who did considerable work on acacia during the war, whether acacia can have a deleterious effect, as it can be demonstrated in the tissues two or three years after it is injected. He felt that he did not have any deleterious effects. What preparation of acacia has Dr. Butt been using in this work? I have not used acacia because of the fear of harmful effects and the possibility of immediate reactions.

DR. EDMUND A. FOLEY, Chicago: I have some sections showing how the liver resembles loose cotton following the intravenous injection of acacia over a period of time. I have particularly noticed that following injections of acacia the serum protein would decrease. It may be 7 Gm. before injection and shortly afterward down to 4 Gm. per hundred cubic centimeters. I have not had the opportunity to try this in cirrhosis of the liver. I am therefore interested to know whether the determinations of serum acacia and serum protein were made following injection in cases of cirrhosis.

DR. HUGH R. BUTT, Rochester, Minn.: Concerning normal colloid osmotic pressure in patients who have ascites and edema, such an instance has been reported by Krogh but the diagnosis was somewhat uncertain. Keith and Binger and others have reported cases of edema of indeterminate origin in which all the constituents of the blood, including proteins, were present apparently within normal limits of concentration. We have made no attempt to determine the molecular size of proteins with which we were dealing. Krogh and his co-workers in their early work attempted to determine the size of particles by varying the permeability of the collodion membranes employed, but because of technical difficulties this effort was abandoned. The only reason I mentioned acacia was to demonstrate that for a short time acacia increases the colloid osmotic pressure of the serum under these circumstances. Clinically, no striking improvement was noted in the few cases that I have mentioned. Acacia has been used by Landis and by Binger and Goudschmidt in an effort to relieve nephrotic patients of edema. They have had varying degrees of success. Coburn and Ward in 1925 reported 1,000 successful cases in which 6 per cent acacia saline solution was used without a single fatality, and in 1932 Maytum and Magath reported that 3,000 injections of acacia solution had been given at the Mayo Clinic and that only one slight reaction had occurred. This reaction was apparently due to the presence of some foreign protein in the solution of acacia. Most solutions of acacia do contain a small percentage of nitrogen. The acacia used at the Mayo Clinic is prepared in Dr. Osterberg's laboratory from crude gum arabic. I believe that most acacia is imported from the Malay States and Africa. It is best given to patients in 6 per cent acacia saline solution, and in none of the cases in which I have used it have I noticed any reaction. The material must be freshly prepared, because I have noticed that when even autoclaved solutions are kept in the icebox for several weeks a moldy material collects in the bottle. Dr. Foley has stated that in dogs given solution of acacia he has been able to produce rather severe damage to the liver. I wonder what amount of acacia he gave to his dogs.

DR. FOLEY: One hundred grams.

DR. BUTT: That is a much larger dose than we give to man under ordinary circumstances. Serum protein in these patients did not show any appreciable decrease after injection of 300 cc. of acacia solution on three successive days. The slight drop in total proteins and in albumin might be attributed to dilution of the blood. In two of these three cases the amount of acacia in the blood stream was determined by Dr. Powers and the decrease in the acacia percentage in the blood paralleled somewhat the decrease in the colloid osmotic pressure. Dr. Keith and his co-workers have reported finding traces of acacia in patients several years after the acacia solution was administered.

Experimental Cirrhosis: Relation of Hepatic Damage and Plasma Proteins to Ascites

DR. JESSE L. BOLLMAN, Rochester, Minn.: Experimental cirrhosis was produced in dogs by long continued administration of carbon tetrachloride. Spontaneous ascites occurred only after extensive hepatic damage and was associated with definite changes in the plasma proteins. Moderate plasmapheresis produces ascites in cirrhotic dogs. The extent of the alterations of the serum proteins necessary to produce ascites appears to be inversely proportional to the extent of hepatic damage present.

V 11
1938

Current Medical Literature

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

Alabama Medical Association Journal, Montgomery

7: 249-280 (Jan.) 1938

The Patient as a Personality. F. A. Kay, Tuscaloosa.—p. 249.
Treatment of Fractures of Surgical Neck and Shaft of Humerus. A. C. Jackson, Jasper.—p. 253.
*Mechanical Treatment of Cervical Arthritis. S. R. Terhune, Birmingham.—p. 255.
Management of Occiput Posterior Positions. T. L. Bennett Jr., Florence.—p. 256.
Sterility: Study with Uterotubal Insufflation Apparatus: A Few Male Faults Mentioned. G. F. Douglas, Birmingham.—p. 259.

Mechanical Treatment of Cervical Arthritis.—Terhune has had twenty-one cases presenting symptoms of pain in the cervical region, shoulder girdle, arm or, more rarely, the precordium, referred to him for "neck stretching," as described by Hanflig in THE JOURNAL Feb. 15, 1936, page 523. After careful examination of each patient he subjected ten to repeated neck stretchings. These ten showed, by x-ray examination, definite signs of cervical arthritis. All have obtained some measure of relief. The other eleven, a few of whom had x-ray evidence of cervical arthritis, also demonstrated active foci of infection in the form of tonsillitis, pharyngitis or sinusitis and were referred to other physicians for eradication of these foci. All these patients have obtained relief from their pain after elimination of the infection. The use of "neck stretching" as a differential diagnostic test, in cases of demonstrable cervical arthritis in the presence of an active focus, is conceivably logical and has been used in one case. Three series of neck stretchings gave no relief and so it was assumed that the pain was not due to root pressure. Tonsillectomy was advised and done three weeks later with complete alleviation of pain shortly afterward.

American Heart Journal, St. Louis

14: 643-788 (Dec.) 1937

Study of Renal Arteries in Relation to Age and to Hypertension. R. H. Williams and T. R. Harrison, Nashville, Tenn.—p. 645.
*Results from Trichlorethylene Inhalations in Anginal Syndrome of Coronary Sclerosis. F. A. Willius and T. J. Dry, Rochester, Minn.—p. 659.
Hemodynamic Studies in Experimental Coronary Occlusion: IV. Stellate Ganglionectomy Experiments. G. Schauer, L. Gross and L. Blum, New York.—p. 669.
Electrocardiographic Changes in Dog Following Sudden Occlusion of Left Anterior Descending Coronary Branch Under Various Experimental Conditions. L. Gross and B. Calef, New York.—p. 677.
Infarction of the Heart: Morphologic and Clinical Appraisal of 300 Cases: Part I. Predisposing and Precipitating Conditions. W. B. Bean, Boston.—p. 684.
Incidence of Myocardial Infarction Without Pain in 200 Autopsied Cases. J. A. Kennedy, Boston.—p. 703.
Thiocyanate Therapy in Hypertension Including a New Micromethod for Determining Blood Thiocyanates. J. Q. Griffith Jr. and M. A. Lindauer, with technical assistance of R. Campbell, Philadelphia.—p. 710.
Reciprocal Rhythm in Patient with Congenital Heart Disease. F. B. Cutts, Providence, R. I.—p. 717.
Studies of Collateral Circulation Following Experimental Vascular Occlusion. I. D. Stein, Mount Vernon, N. Y.—p. 726.
Complete Auriculoventricular Block and Auricular Flutter with Observations of Effect of Quinidine Sulfate. L. F. Jourdonais and H. O. Mosenthal, New York.—p. 735.

Trichlorethylene Inhalations in Anginal Syndrome.—In determining the effect of inhalations of trichlorethylene on the anginal syndrome of coronary sclerosis, Willius and Dry observed forty such patients. Sixteen months has elapsed since the beginning and five months since the close of the observation. With three exceptions the patients remained ambulatory and were away from home and their accustomed responsibilities and may have been under conditions more conducive to rest and relaxation than would be the case were they treated in their respective communities. The results do not permit this method of treatment to be accepted with enthusiasm. In eighteen cases varying degrees of improvement occurred. However, when the results are analyzed critically it is found that only one patient obtained complete relief, while the others had fewer attacks of less severity. In five cases temporary improvement was noted, but a return of the previous symptoms occurred while the treatment was still in progress. It is possible that a new hope in undertaking the treatment influenced this attitude, although care was taken not to create any false hopes. In thirteen cases no improvement was observed. These patients received treatment from one to seven months. Four patients died during the course of treatment. All deaths occurred suddenly. Two of the patients who died were temporarily benefited. While the results obtained with this method of treatment have been disappointing, it is however a procedure that warrants a trial when the usual therapeutic agents have failed to give relief. The drug is well tolerated and its administration appears to be perfectly safe.

American Journal of Public Health, New York

28: 1-116 (Jan.) 1938

An Equal Opportunity for Health. H. H. Lehman, Albany, N. Y.—p. 1.
Familial Aggregation of Infectious Diseases. W. H. Frost, Baltimore.—p. 7.
A State Cancer Program. H. D. Chadwick and H. L. Lombard, Boston.—p. 14.
Diabetes: An Important Public Health Problem. C. F. Bolduan, New York.—p. 21.
Determining Population in Intercensal and Postcensal Years by Means of Continuous Population Registers. Dorothy Swaine Thomas, New Haven, Conn.—p. 28.
Epidemic Diarrhea of the New-Born: III. Epidemiology of Outbreaks of Highly Fatal Diarrhea Among New-Born Babies in Hospital Nurseries. S. Frant and H. Abramson, New York.—p. 36.
*Experiments on Antirabic Vaccination with Tissue Culture Virus. L. T. Webster, New York.—p. 44.
*Relation of Lymphocytic Choriomeningitis to Acute Aseptic Meningitis (Wallgren). R. D. Baird and T. M. Rivers, New York.—p. 47.
Difficulties Encountered in Pneumococcic Type Determination. Annabel W. Walter, New York.—p. 54.
Alpha Hemolytic Streptococci of Air: Their Variant Forms, Origin and Numbers per Cubic Foot of Air in Several Types of Locations. L. Buchbinder, Mathilde Solowey and M. Solotorovsky, New York.—p. 61.
Nutrition and Dental Caries. B. R. East, Harrison, N. J.—p. 72.

Antirabic Vaccination with Tissue Culture Virus.—To find a safe and effective antirabic vaccine, Webster carried out the following experiments: Mice of a selected Swiss strain were chosen as test animals. The mice could be readily immunized against an intracerebral injection of test virus containing up to 10,000 lethal doses. A single intraperitoneal injection of at least 1,000 intracerebral lethal doses rendered mice resistant within fourteen days and over a period of at least nine months. Neutralizing antibodies were likewise present. Various commercial preparations were then examined with respect to their immunizing capacities. None immunized the mice when given according to directions in a single dose in a quantity at least ten times that administered to dogs per gram of body weight. The possibility of a new source of vaccine was investigated. Preparations in current use are composed largely of virus-containing brain or cord tissue of rabbits, sheep or monkeys. In 1936, however, the propagation of rabies virus in culture mediums outside the animal body was reported by Kanazawa and by Webster and Clow. The author's cultures have been continued unremittingly now for ninety-five passages and have become uniformly virulent through the 1:10,000 dilution. This culture virus was tested for its ability to immunize mice. Of the undiluted culture, 0.25 cc., equal to 80,000 intracerebral lethal doses, was harmless when injected intraperitoneally and protected the mice in fourteen days against an intracerebral test injection of 1,000 lethal doses of mouse brain virus. One tenth of this amount of culture vaccine was likewise effective, but one one-hundredth, containing only 800 lethal doses, was insufficient for immunization. Immunity, when produced, endured at least nine months and was accompanied by protective antibodies. Attempts were then made with culture virus to immunize beagle puppies. Dogs were vaccinated with relatively small amounts of culture virus, from 5,000 to 20,000 lethal mouse doses, barely twenty times that required to immunize mice. The vaccine

has proved harmless to all forty-five dogs thus far treated and has immunized them as follows: Fourteen vaccinated dogs resisted one lethal dose of test skunk virus fatal to nine of eleven controls. Likewise, three of six vaccinated dogs resisted ten lethal doses fatal to all five tested controls. The 15,000 lethal mouse doses of culture vaccine which immunized dogs against one test lethal brain dose can be contained in 1 cc. and can be increased apparently without harm to 1,000,000 lethal mouse doses. With a larger amount of lethal mouse doses in the vaccine a greater resistance is expected.

Relation of Lymphocytic Choriomeningitis to Acute Aseptic Meningitis.—Baird and Rivers present evidence (sixty-five cases) which indicates that not all cases of acute aseptic meningitis (Wallgren) are caused by the virus of lymphocytic choriomeningitis. The etiologic agent or agents responsible for the cases not so induced are not known. From the records of three patients with lymphocytic choriomeningitis it appears that certain cases of the disease, because of the extent of paralysis and sequels, do not satisfy the criteria laid down by Wallgren for the diagnosis of acute aseptic meningitis. It is difficult or impossible to differentiate by clinical means alone the cases of acute aseptic meningitis caused by the virus of lymphocytic choriomeningitis from those not produced by the agent; however, the spinal fluid cell counts in the cases studied tend to be higher in the former group than in the latter. Children and even infants are not infrequently attacked by the virus of lymphocytic choriomeningitis.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

39: 1-160 (Jan.) 1938

Treatment of Carcinoma of the Breast: Caldwell Lecture, 1937. G. E. Pfahler, Philadelphia.—p. 1.
Roentgenologic Recognition of Certain Bronchomycoses Involving Occupational Risks. R. Fawcitt, Ulverston, England.—p. 19.
The Normal Skull: From a Roentgenologic Point of View. C. W. Schwartz, New York.—p. 32.
Isolated Fractures of Vertebral Arch. G. Steiner, Teplitz-Schönau, Czechoslovakian Republic.—p. 43.
Roentgen Diagnosis of Osteomyelitis of Vertebrae. J. R. McNutt, Duluth, Minn.—p. 52.
Submentovertex View as an Aid in Mastoid Roentgenography. S. W. Westing, Brooklyn.—p. 59.
Motility of Gastro-Intestinal Tract. R. P. Wallace, I. Ehrenfeld, M. P. Cowett, N. Joliffe, L. L. Shapiro and M. Sturtevant, New York.—p. 64.
Phytobezoar: Report of Three Cases. L. G. Allen, Kansas City, Kan.—p. 67.
Use of Radium and Roentgen Irradiation in Benign Hypertrophy and Cancer of the Prostate. C. F. Burnam, Baltimore.—p. 75.
Serum Therapy in Cancer. I. I. Kaplan and Anna Goldfeder, New York.—p. 84.
Therapeutic Uses of Estrin. C. F. Geschickter, Baltimore.—p. 90.
*Massive Roentgen Irradiation of Hypophysis in Experimental Diabetes. J. B. Johnson, W. A. Selle and J. J. Westra, Galveston, Texas.—p. 95.
Diffraction Studies of Effect of Sodium Fluoride and Parathormone on Incisors and Tibiae of Rats. L. Reynolds, K. E. Corrigan, Henrietta S. Hayden, Icie G. Macy and Helen A. Hunscher, Detroit.—p. 103.

X-Ray Irradiation of Hypophysis in Experimental Diabetes.—Since the hypophysis elaborates a diabetogenic hormone and its removal reduces the severity of experimental diabetes, Johnson and his co-workers thought that heavy doses of x-rays directed to the gland might produce similar results. Seven dogs were rendered diabetic by removal of the pancreas. After recovery from the operation the animals were kept on a basic diet of dog biscuits, sugar and ground meat, to which were added liberal amounts of fresh or dried pancreas. On this stock diet 2 units of insulin per kilogram of body weight was given twice daily at the time of feeding. The animals were seldom given sufficient insulin to render them sugar free, yet they were never permitted to show marked glycosuria or ketonuria. Prior to periods when the tolerance to dextrose and insulin was determined, the animals were maintained in a constant diabetic state. To test the animal's sensitivity to insulin, food and insulin were withheld for twenty hours during the period of controlled diabetic state. From 2 to 2½ units of insulin was then administered and the animal was observed over a period of four hours to see whether convulsions occurred. Following control tolerance tests, the animals were given varying doses of x-rays to the hypophysial area through one dorsal and two lateral portals, each 5 cm. square. The physical constants employed were 140 kilovolts (mechanical rectification) with 5 milliamperes, a focal skin distance of 50 cm., 0.5 mm. of copper and 1 mm. of aluminum filtration. With these constants the Coolidge tube delivered 5.8 roentgens per minute. The total dose given the hypophysis varied between 750 and 2,025 roentgens for a single treatment. Subsequent dextrose and insulin tolerance tests were carried out at weekly intervals following irradiation. The data show a wide variation in the fasting blood sugar of most of the animals following irradiation. The irradiation did not render the animals hypersensitive to insulin during fasting, for convulsions never occurred in any of the animals given 2 units of insulin per kilogram of body weight, and all animals but one tolerated 2.5 units. Glycosuria was not greatly reduced by irradiation. The two heaviest irradiated animals eliminated dextrose in amount nearly maximal for starving depancreatized animals. Microscopic studies made on six of the seven animals irradiated indicate that the hypophysis was seriously damaged by the treatment. The gland was impaired in four, as indicated by edema and degeneration of the cells of the pars tuberalis. The nerve structures of the brain, however, showed more clearly the effects of the massive irradiation. Thus, the cortex of all animals and the midbrain of those animals receiving 1,500 roentgens or more of radiation were definitely damaged.

American Journal of Surgery, New York

39: 1-226 (Jan.) 1938

Diaphragmatic Hernia: Review of Literature. A. Bowen, Los Angeles.—p. 4.
Wounds of Thoracic Viscera. F. B. Berry, New York.—p. 12.
Conditions Erroneously Diagnosed as Appendicitis. C. G. Heyd, New York.—p. 18.
Appendicitis from Histologic Standpoint. S. W. Sappington and J. A. Horneff, Philadelphia.—p. 23.
Plexiform Neuroma of Appendix: Study of 600 Appendixes. M. J. Fein, J. T. Hanan and V. B. Seidler, Brooklyn.—p. 27.
Intestinal Tuberculosis. J. K. Miller, Louisville, Ky.—p. 34.
Study Regarding Abdominal Adhesions and of Cotton and Gauze Sponges. J. K. Donaldson, Little Rock, Ark.—p. 37.
Some Practical Experiences in Construction of Abdominal Supports. J. Wolf, Davenport, Iowa.—p. 42.
Major Lower Extremity Amputations in the Aged Poor-Risk Patient. R. T. Findlay, New York.—p. 46.
Breast Deformities: Anatomic and Physiologic Considerations in Plastic Repair. J. W. Maliniac, New York.—p. 54.
"Bloodless" Cesarean Section. R. L. Gorrell, Clarion, Iowa, and F. L. Wilson, Stuart, Neb.—p. 62.
Genito-Urinary Tuberculosis. J. K. Miller, Louisville, Ky.—p. 67.
Renal Infarcts: Surgical Aspect of Bacterial Endocarditis. J. Schwartz, New York.—p. 70.
Transurethral Prostatic Resection: Report of 101 Operations on Eighty-Six Cases. F. C. Hamm, Brooklyn.—p. 77.
*Eucupine (Isoamylhydrocupreine) as Local Anesthetic in Proctologic Surgery and in Treatment of Pruritus Ani. S. D. Manheim, New York, and M. M. Marks, Kansas City, Mo.—p. 86.
Supervoltage X-Ray Therapy. F. W. O'Brien, Boston.—p. 95.
*Sex Hormone Therapy for Prostatism. R. V. Day, H. W. Martin, A. A. Kutzmann and E. E. Kessler, Los Angeles.—p. 100.
Recurrent and Continuing Hyperthyroidism. T. O. Young, Duluth, Minn.—p. 104.
Observations on Solutions Used for Injection Treatment of Hernia. F. I. Harris, A. S. White and G. R. Biskind, San Francisco.—p. 112.
New Sclerosing Drug for Varicose Veins—Monolate. S. T. Glasser, New York.—p. 120.

Eucupine as Anesthetic in Treatment of Pruritus Ani.—Manheim and Marks found 0.1 per cent eucupine dihydrochloride with 1 per cent procaine hydrochloride in saline solution a reliable anesthetic for minor rectal surgical procedures. Anesthesia is rapid and is not attended by tissue reactions, irritation or evidence of any systemic effects. The anesthesia and postoperative analgesia produced persist from three to seven days without the addition of epinephrine. The employment of this solution requires no special technic and it can be used to maintain prolonged regional anesthesia as a supplement to inhalation, spinal or intravenous anesthesia. No evidence of delayed healing has been encountered. Eucupine in oil requires special technic in its use to avoid pooling. The formula has been employed successfully in a variety of anal conditions both for treatment and for surgical repair. Its greatest value is in the treatment of pruritus ani, as the infiltration may be repeated as often as the condition demands. The analgesic effect of a single injection usually persists from two to six weeks, and local tissue reactions are rare when the substance is properly used.

V 11
1938

Endocrine Therapy for Prostatism.—Day and his colleagues state that two testicular hormones have been isolated in pure crystalline form, androsterone and testosterone, the exact chemical constitutions of which have been determined, and have both been prepared synthetically, together with a number of intermediate substances. Their clinical results in forty cases practically parallel those of Lower, Van Capellen and Laqueur and show some clinical improvement in about 50 per cent of carefully selected patients, whose residual urine did not exceed 100 cc. Most of their observations during the past fifteen months have been based on the clinical use of the synthetic testosterone propionate. The preparation is dissolved in oil of sesame and is nonirritating when injected intramuscularly. Use of this substance is frequently invaluable in feeble and very old men to tide them over certain emergencies, such as cystostomies, which may be imperative. It may be used to advantage in castrates. The use of testosterone is seemingly effective in bringing about clinical improvement in a large percentage of patients with benign prostatic hypertrophy, in inhibiting hyperplasia and holding it in check at least temporarily. Its use is still in the experimental stage, and more clinical and experimental data are necessary before definite conclusions can be ventured.

Archives of Internal Medicine, Chicago

61: 1-160 (Jan.) 1938

Pulmonary Arteriolar Sclerosis: Clinicopathologic Study. D. H. Kaump and T. J. Dry, Rochester, Minn.—p. 1.
Severe Anemia of Aplastic Type Associated with Sclerosis of Thyroid Gland. R. H. Jaffé, Chicago.—p. 19.
*Gonococcic Endocarditis: Study of Twelve Cases, with Ten Postmortem Examinations. R. H. Williams, Nashville, Tenn.—p. 26.
Mitral Stenosis: Correlation of Electrocardiographic and Pathologic Observations. K. Berliner and A. M. Master, New York.—p. 39.
Gastro-Intestinal Manifestations of Lymphogranulomatosis (Hodgkin's Disease). E. D. Sherman, Sydney, Nova Scotia.—p. 60.
*Immediate Effect of Tincture of Digitalis on Emptying Time of Human Stomach. E. J. Van Liere and C. K. Sleeth, Morgantown, W. Va.—p. 83.
Urea Clearance in Pernicious Anemia. P. J. Fouts and O. M. Helmer, Indianapolis.—p. 87.
Experimental Endocarditis Due to Streptococcus Viridans: Biologic Factors in Its Development. M. Friedman, L. N. Katz and K. Howell, with collaboration of E. Lindner and M. Mendlowitz, Chicago.—p. 95.
Experimental Peptic Ulcer Produced by Cinchophen. J. L. Bollman, L. K. Stalker and F. C. Mann, Rochester, Minn.—p. 119.
Allergy: Review of Literature of 1937. F. M. Rackemann, Boston.—p. 129.

Gonococcic Endocarditis.—Williams comments on twelve cases of gonococcic endocarditis, in ten of which a postmortem study was made. Gonococcic endocarditis constituted 26 per cent of all instances of acute bacterial endocarditis in patients admitted to the Vanderbilt University Hospital in the last twelve years. It was observed in 0.7 per cent of 1,719 necropsies performed during this period. It occurred in all age groups and was more frequent in men. The onset was sometimes insidious, consisting of generalized aching, malaise and fever. In other patients there occurred high fever, chills, petechiae and articular pains. Acute polyarthritis was usually the first focal manifestation of generalized gonococcic infection. Petechiae usually occurred early in the disease and frequently recurred in showers. Large petechiae with necrotic centers are suggestive of endocarditis. Renal complications, frequently embolic, were commonly present. The temperature usually showed marked daily fluctuations. Signs of valvular disease appeared in every instance during the illness. Myocarditis sometimes occurred. The liver and spleen were often enlarged, and jaundice was present in five instances. Marked leukocytosis and moderate or severe anemia occurred. The urine frequently contained moderate amounts of albumin, red blood cells, white blood cells and casts. Uremia was a common development and was the main cause of death in 42 per cent of the patients. The average duration of the endocarditis was five weeks. A correct diagnosis of gonococcic endocarditis can be established only after close clinical observation and careful bacteriologic studies. Repeated cultures on special mediums are often necessary to recover gonococci from the blood. Electropyrexia and chemotherapy (sulfanilamide) seem to offer some therapeutic promise.

Effect of Digitalis on Emptying Time of Stomach.—Van Liere and Sleeth found that 5 cc. of tincture of digitalis when mixed with a standard test meal (consisting principally of 15 Gm. of farina) decreased the normal emptying time of the stomach on an average of 18.5 per cent in seven healthy young men. In no case was the decrease in the emptying time less than 12.9 per cent, and the greatest decrease noted was 24.6 per cent. Since tincture of digitalis appears capable of decreasing the emptying time of the stomach, it may be given immediately before or directly after a meal without any deleterious effect on gastric motility. Experimental evidence is offered which throws light on the causation of the diarrhea which often accompanies the administration of digitalis. Since digitalis is often given in conditions associated with anoxemia, which has been shown to inhibit gastric motility, the fact that it is capable of decreasing the emptying time of the stomach is of practical importance.

Arch. of Physical Therapy, X-Ray, Radium, Chicago

19: 1-64 (Jan.) 1938

Deformities Following Fracture: Their Prevention and Treatment. M. S. Henderson, Rochester, Minn.—p. 7.
Short Wave Treatment of Endocrine System, Diencephalon and Mesencephalon. J. Samuels, Amsterdam, Netherlands.—p. 13.
Relation of Autonomic Nervous System to Physical Therapy. A. Kuntz, St. Louis.—p. 24.
Elliott Treatment in Prostatic Disorders. L. W. Riba and C. Vance, Chicago.—p. 29.
Electrocoagulation in Bronchogenic Conditions. J. D. Kernan, New York.—p. 38.
Restoration of Muscle Balance in Treatment of Sciatic Pain. R. E. Lenhard and H. O. Kendall, Baltimore.—p. 44.

Delaware State Medical Journal, Wilmington

10: 1-18 (Jan.) 1938

Practical Points in Relation to Clinical Surgery. W. W. Babcock, Philadelphia.—p. 1.

Endocrinology, Los Angeles

22: 1-154 (Jan.) 1938

*Effects of Parathyroid Extract and of Vitamin D on Blood Phosphatase, Calcium and Phosphorus in Osteogenesis Imperfecta. A. E. Hansen, I. McQuarrie and Mildred R. Ziegler, Minneapolis.—p. 1.
Experimental Acute Hyperparathyroidism: II. Morphologic Changes. A. Cantarow, H. L. Stewart and E. L. Housel, Philadelphia.—p. 13.
Relative Effectiveness of Emmenin, Estriol Glycuronide and Estriol in Immature and Castrate Immature Rat. R. R. Greene and A. C. Ivy, Chicago.—p. 28.
Changes in Electrical Potential During Estrous Cycle of Rat: II. Partial and Complete Hypophysectomy and Pituitary Replacement Therapy. P. V. Rogers, New Haven, Conn.—p. 35.
*Estimation of Ovarian Activity by Consecutive-Day Study of Basal Body Temperature and Basal Metabolic Rate. B. B. Rubenstein, Cleveland.—p. 41.
Use of Adrenal Cortex Preparations in Treatment of Asthenia. E. S. Gordon, E. L. Sevringhaus and Marian E. Stark, Madison, Wis.—p. 45.
Further Observations on Relation of Adrenal Cortex to Experimental Diabetes. F. D. W. Lukens and F. C. Dohan, Philadelphia.—p. 51.
Further Observations on Treatment of Hypogenitalism and Undescended Testes, with Especial Reference to Production of Premature Puberty. W. O. Thompson, N. J. Heckel, P. K. Thompson and L. F. N. Dickie, Chicago.—p. 59.
Relation of Thyroid Gland to Spontaneous Activity of the Rat. V. E. Hall and Margaret Lindsay, Stanford University, Calif.—p. 66.
Effect of Thyrotropic Hormone, Alone and with Other Substances, on the In Vitro Oxygen Consumption of Thyroid and Liver. A. Canzanelli and D. Rapport, Boston.—p. 73.
Anterior Pituitary Factor Which Maintains Muscle Glycogen in Fasted Hypophysectomized Rats. Jane A. Russell, Berkeley, Calif.—p. 80.
Analysis of Amenorrhea by Use of Commercial Prolactin and Luteinizing Hormone. I. T. Nathanson and H. L. Fevold, Boston.—p. 86.
Influence of Light on Hypophysis: Effects of Long Continued "Night Lighting" on Hypophysectomized Female Ferrets and Those with Optic Nerves Cut. T. H. Bissonnette, Hartford, Conn.—p. 92.

Parathyroid Extract and Vitamin D in Osteogenesis Imperfecta.—Hansen and his associates investigated the effects of parathyroid extract and of large doses of viosterol on the phosphatase activity of the blood in four cases of osteogenesis imperfecta, correlating results with possible changes in the calcium, phosphorus and proteins of the serum and with variations in the calcium and phosphorus balances measured simultaneously. The ages of the patients were 12, 3, 9 and 7 years, respectively. The plasma phosphatase activity of these patients was found to be within normal limits under ordinary conditions

but was greatly depressed by both parathyroid extract and viosterol. The serum calcium, on the other hand, was definitely increased by both agents. The inorganic phosphorus of the serum was decreased by the administration of parathyroid extract in three cases and increased slightly in one. The level of serum inorganic phosphorus was not significantly altered by the viosterol except in the case of the youngest patient. In this instance it was merely increased from a subnormal to a normal level. The serum proteins were unchanged by either parathyroid extract or viosterol. Generally, the effects of parathyroid extract and of large doses of viosterol were alike in producing negative balances of phosphorus and calcium in these cases as they do in normal subjects. Such agents are therefore contraindicated in osteogenesis imperfecta because they tend to accentuate the functional disturbance already present. Therapeutic procedures which would increase the phosphatase activity might, on the other hand, have a beneficial effect in this disorder.

Ovarian Activity and Basal Metabolic Rate.—The existence of the temperature cycle suggested the possibility that a metabolic cycle might also be present. Rubenstein presents the data in a study of the basal metabolism rate of fifteen young adult women. The basal metabolic rate was taken in duplicate, the Benedict-Roth machine being used and the usual precautions being taken. The basal metabolic rate fluctuates widely but regularly during the menstrual cycle, the lowest values occurring just before the middle period (about the thirteenth day of a twenty-eight day cycle). The basal body temperature also varies in the same way, the low point coinciding with the most highly cornified (ovulative) vaginal smear. Body temperature and basal metabolic rate seem to be equivalent measures of ovarian activity.

Georgia Medical Association Journal, Atlanta

27: 1-42 (Jan.) 1938

First Aid Treatment and Transportation of Fractures. G. N. Coker, Canton.—p. 1.
Importance of X-Ray Examination of Fractures. H. H. McGee, Savannah.—p. 4.
Treatment of Fractures in a Small Hospital. C. Thompson, Millen.—p. 7.
Treatment of Compound Fractures. R. L. Rhodes, Augusta.—p. 8.
The After-Care of Fractures. M. Hoke, L. Thornton and C. Sandison, Atlanta.—p. 10.
Diagnosis and Treatment of Acute Head Injuries. H. L. Cheves, Union Point.—p. 13.
Medicolegal Aspects of Fractures. G. Middlebrooks, Atlanta.—p. 15.
Review of Complications Following Administration of Sulfanilamide. A. P. McGinty, Atlanta.—p. 21.

Journal of Biological Chemistry, Baltimore

122: 275-596 (Jan.) 1938. Partial Index

Form of Copper in Blood Plasma. Ruth Boyden and V. R. Potter, Madison, Wis.—p. 285.
Activation of Testosterone by Higher Fatty Acids and Their Acid Sodium Salts. M. Ehrenstein and E. L. Corey, University, Va.—p. 297.
Isolation of Estrogenic Diols from Urine of Pregnant Mares. H. Hirschmann and O. Winterstein, New York.—p. 303.
Role of Acetyl Derivative as an Intermediary Stage in Biologic Synthesis of Amino Acids from Keto Acids. V. du Vigneaud and O. J. Irish, Washington, D. C.—p. 349.
Studies on Constitution of Insulin: III. Acetylation of Insulin by Ketene. K. G. Stern and A. White, New Haven, Conn.—p. 371.
Relation of Fat to Utilization of Lactose in Milk. E. J. Schantz, C. A. Elvehjem and E. B. Hart, Madison, Wis.—p. 381.
Do Androgens Affect Blood Lipids? C. D. Kochakian, P. L. MacLachlan and H. D. McEwen, Rochester, N. Y.—p. 433.
Observations on Relation Between Ionized and Total Calcium in Normal and Abnormal Serums and Their Ultrafiltrates. R. S. Morison, Regina McLean and Elizabeth B. Jackson, Boston.—p. 439.
Extracellular and Intracellular Water in Bone and Cartilage. Vivian Job and W. W. Swanson, Chicago.—p. 485.
Further Determination and Characterization of Component Acids of Butter Fat. T. P. Hilditch and H. E. Longenecker, Liverpool, England.—p. 497.
Method for Preparation of Posthemolytic Residue or Stroma of Erythrocytes. S. S. Bernstein, R. L. Jones, Betty Nims Erickson, H. H. Williams, I. Avrin and Icie G. Macy, Detroit.—p. 507.
Lipid Distribution of Posthemolytic Residue or Stroma of Erythrocytes. Betty Nims Erickson, H. H. Williams, S. S. Bernstein, I. Avrin, R. L. Jones and Icie G. Macy, Detroit.—p. 515.
Effect of Dibenzanthracene on Vitamin A and Total Lipid of Mitochondria. A. Goerner, Brooklyn.—p. 529.
Determination of Sulfanilamide (*p*-Aminobenzenesulfonamide) in Biologic Mediums. J. V. Scudi, New York.—p. 539.

Journal of Bone and Joint Surgery, Boston

20: 1-262 (Jan.) 1938. Partial Index

Scoliosis Treated by the Wedging Jacket: Selection of Area to Be Fused. F. L. Butte, New York.—p. 1.
Tuberculous Osteitis of Ischium. R. Magnusson, Borås, Sweden.—p. 23.
Acute Hematogenous Osteomyelitis. D. E. Robertson, Toronto.—p. 35.
*Chondrodysplasia (Ollier's Disease): Report of Case Resembling Osteitis Fibrosa Cystica. G. H. Sanderson, Stockton, Calif., and F. S. Smyth, San Francisco.—p. 61.
Spinal Fixation: Method of Bending the Graft. G. Hamada, Alexandria, Egypt.—p. 85.
Reconstruction Operations for Old Ununited Fractures of Neck of Femur. E. G. Brackett, Boston.—p. 93.
Comments on Internal Fixation in Fresh Fractures of Neck of Femur. W. W. Plummer, Buffalo.—p. 97.
*Dashboard Dislocation of Hip: Report of Twenty Cases of Traumatic Dislocation. R. V. Funsten, P. Kinser and C. J. Frankel, Charlottesville, Va.—p. 124.
The Spastic Hand. M. S. Burman, New York.—p. 133.
Spastic Intrinsic-Muscle Imbalance of the Foot: Resection of Motor Branch of Lateral Plantar Nerve for Intrinsic-Muscle Contracture. M. S. Burman, New York.—p. 145.
*Use of Amniotic Fluid Concentrate in Orthopedic Conditions. M. Shimberg, Wadsworth, Kan.—p. 167.
Fractures of Metacarpals: New Method of Reduction and Immobilization. S. A. Jahss, New York.—p. 178.
Tendon Transposition: End-Result Study. C. W. Peabody, Detroit.—p. 193.
Friction versus Traction: Simple Appliance for Use in Making Traction to the Head. A. H. Freiberg, Cincinnati.—p. 213.
Peroneal Nerve Palsy Due to Compression by Adhesive Plaster. S. Selig, New York.—p. 222.
Adaptation of Balkan Frame for Developing Motion and Abduction of Hip. P. L. Norton and F. Ilfeld, Boston.—p. 224.
New Technic in Treatment of Fractures of the Forearm. L. Zeno, Rosario, Argentine Republic.—p. 229.

Chondrodysplasia (Ollier's Disease).—Sanderson and Smyth report a case in which the resemblance of chondrodysplasia to osteitis fibrosa cystica might lead to confusion as to the diagnosis. The involvement is both symmetrical (legs) and asymmetrical (arms) and clearly demonstrates that symmetry is of no diagnostic import. The disease consists of cartilaginous lesions, which tend to become grouped, first, in the individual long bones, and, second, in the extremities. When more than one extremity is involved, the tendency to affect whole extremities naturally results in either symmetry or asymmetry. The disease runs a characteristic course and reaches a stage in which the ends of some of the long bones become expanded, grossly deformed and shortened. In the case reported, the deformity became evident at the third year but did not become prominent until later. There was a gradual steady increase in the extent of the individual lesions, as well as some spread in their distribution. There is at no time in the course of the disease a stage in which it resembles multiple cartilaginous exostoses, called also "hereditary deforming chondrodysplasia." Differentiating Ollier's disease on the basis of asymmetrical distribution adds to the confusion. It would seem much more logical to group all the endochondral cases under the term "Ollier's disease" or possibly "endochondrodysplasia." Those associated with exostoses or ecchondral cases could then be termed "ecchondrodysplasia." The calcium balance in the case reported was within normal limits, thus further differentiating the condition from osteitis fibrosa cystica, which it resembles slightly. This would indicate that, if any enlarged parathyroids are found in such cases, they are due to secondary hyperplasia and should not be removed. Treatment at the present time is largely that of corrective orthopedics.

Dashboard Dislocation of Hip.—Funsten and his associates use the name "dashboard" dislocation of the hip because the person so injured was usually sitting beside the driver of an automobile when it came to an abrupt stop in a collision. In such a case, since the hip is in a flexed and adducted position, the force of the impact of the tibia or of the knee against the panel is transmitted through the femur to the posterior rim of the acetabulum, and the result may be a simple dislocation or a dislocation with fracture of the lip of the acetabulum. Occasionally a fracture of the tibia or of the patella is experienced instead. This mechanism was the cause of dislocation in thirteen of the twenty cases reported. In the remaining seven, two patients were thrown out of automobiles, two were struck by automobiles, one patient fell from a tree, one fell from a box car and one was injured at birth. The routine method of

treatment in the fresh cases was immediate closed reduction, followed by traction of the Russell or Buck type. If there was a formidable fracture of the acetabulum, the traction was maintained for eight weeks. If, however, no acetabular fracture existed, traction lasted only from two to three weeks. During the period of traction in both instances, active motion was maintained in the knee and the hip joints. Treatment of the old cases required much more active correction, and the results were discouraging. The end results were good in eleven cases, fair in two, poor in five and undetermined in two.

Amniotic Fluid Concentrate in Orthopedic Conditions.—It occurred to Shimberg that if human and bovine amniotic concentrate was effective in hastening the process of repair within the peritoneum it ought to be of value in other serous cavities, including those of the joints of the body. Amniotic fluid concentrate was used within the joint cavities in sixty-eight cases of various pathologic conditions of the joints. The concentrate was obtained by concentrating, fractionating and purifying the amniotic fluid of cows which are from two to four months pregnant. The concentrate appears to influence favorably the mechanism of defense repair. It contains allantoin in small amounts, and allantoin is of value in promoting repair. Amniotic fluid is a body fluid, and one of its functions is to prevent adhesions between the fetus and the amniotic sac. Its use within joint cavities accomplishes several purposes: 1. It distends the cavity with an innocuous fluid, and this mechanical distention separates to some extent the injured surfaces. 2. It excites an immediate defense reaction in the intra-articular tissues, with the formation of much fibrin, and at the same time reduces oozing time to a minimum. As the defense reaction wanes, a repair process is stimulated. Apparently the normal body process of defense and repair is enhanced with a resultant early resolution, thereby limiting fibrous adhesions. 3. The fluid influences intra-articular viscosity, and the lubricant factor in joint function is favorably affected. The results obtained by arthrotomy after injection of this fluid compare favorably with those of others as regards postoperative complications, time of functional restoration and final end results. In fractures of the intra-articular type, there is no doubt that the fluid has definite value. In atrophic arthritis it seems indicated when there is effusion or marked involvement of the synovial membrane. The observations indicate that amniotic fluid concentrate has some value in orthopedic disabilities.

Journal-Lancet, Minneapolis

58: 1-42 (Jan.) 1938

Clinical Significance of Glycosuria. B. A. Watson, Minneapolis.—p. 1.
Complications and Management of Pregnancy and Labor Among Physicians' Wives. R. D. Mussey and J. E. Faber, Rochester, Minn.—p. 5.
Dietary Regimen in Treatment of Renal Calculi. C. C. Higgins, Cleveland.—p. 9.
*Hypertonic Dextrose Solutions in Treatment of Bronchial Asthma. A. V. Stoesser and M. M. Cook, Minneapolis.—p. 12.
Fractures of the Spine. G. A. Williamson, St. Paul.—p. 16.
Homonymous Hemianopsia With and Without Sparing of Macula in Lesions of Visual Cortex. C. Hymes, Minneapolis.—p. 20.
Some Facts and Comments on Physical Therapy: Review of Literature. A. Stolinsky, Lisbon, N. D.—p. 23.

Hypertonic Dextrose Solutions in Bronchial Asthma.—Stoesser and Cook observed three children with histories of bronchial asthma from seven to eight years, in whom epinephrine failed to give satisfactory results, over a period during which they received intravenously hypertonic solutions of dextrose, sodium chloride and sucrose. The asthmatic attacks due to ingestants responded favorably to the dextrose, while those due to inhalants were not controlled satisfactorily. A child without an associated infection tolerated the dextrose solutions much better than the children with secondary infections. The fact that the dextrose was administered as a hypertonic solution did not appear to aid in determining the mechanism of control of the asthma due to food allergy. The sodium chloride solution was not used in the inhalant. Preliminary investigations have shown that high salt diets tend to precipitate attacks of asthma. Hypertonic sucrose solutions, however, were tried as a substitute, but they were unsuccessful in controlling asthmatic attacks. The variation in the response to dextrose depending on the etiology of the asthma may open a new avenue of approach to the study of the underlying mechanism in allergic disease. The severity of the asthmatic attacks in the cases which have not responded satisfactorily to the carbohydrate therapy appears to be influenced by shifts in the sodium chloride intake in the diet. This offers a new form of therapy.

Journal of Pediatrics, St. Louis

11: 743-886 (Dec.) 1937

Acute Infective Polyneuritis in Childhood. M. S. Hecht, Baltimore.—p. 743.
*Dural Sinus Thrombosis in Early Life: I. Clinical Manifestations and Extent of Brain Injury in Acute Sinus Thrombosis. O. T. Bailey and G. M. Hass, Boston.—p. 755.
Epidemic Diarrhea of the New-Born: II. Control and Prevention of Outbreaks in Hospital Nurseries. S. Frant and H. Abramson, New York.—p. 772.
Antirachitic Value of Irradiated Evaporated Milk in Infants: An Outpatient Study. M. Rapoport, Elizabeth Krick and J. Stokes Jr., Philadelphia.—p. 782.
Cretinoid Epiphysial Dysgenesis. W. A. Reilly and F. S. Smyth, San Francisco.—p. 786.
Intracranial Hemangioma Associated with Facial Nevus. A. O. Hecker, Polk, Pa.—p. 797.
Comparative Study of Levinson and Tryptophan Tests as Aids in Diagnosis of Tuberculous Meningitis. F. X. Giustra, Brooklyn.—p. 805.
*Lymphogranuloma Venereum in Childhood: Review of Literature with Report of Case. H. Levy, Brooklyn.—p. 812.
*Drugs Transmitted Through Breast Milk: Part I. Laxatives. R. M. Tyson, E. A. Shrader and H. H. Perlman, Philadelphia.—p. 824.
Further Suggestions for Approaching Children and Their Parents: Part II. E. L. Vincent, Detroit.—p. 833.

Dural Sinus Thrombosis in Early Life.—Bailey and Hass correlate the extent of brain injury with the localization of the thrombi in the venous sinuses and their tributary veins in eighty cases of thrombosis of the dural venous sinuses in children, all but three of whom were less than 3 years of age. Especial attention is given to the large group of infants and children in whom the thrombosis could not be attributed to the localization of a demonstrable infectious agent in the sinus wall or tributary veins. Forty-two cases were associated with various forms of sepsis: meningitis, scalp infections, otitis media, mastoiditis and bacteremias without meningeal localization. Four instances followed surgical procedures. Thirty-three patients presented no evidence of infection of the central nervous system or blood stream. They were all infants less than 30 months of age. The illness began with an acute nutritional disturbance usually followed after a period of days or weeks by evidences of meningeal irritation, marked hyperpyrexia and convulsions or other abnormal neurologic manifestations. Some infants died without any evidence of neurologic disturbance. In all these patients the superior longitudinal sinus was thrombosed in its entirety or in part with variable involvement of other sinuses and cerebral veins. Twenty-one of the patients presented hemorrhages into the meninges associated in nineteen cases with intracerebral hemorrhage and necrosis. Some of the patients succumbed within a few hours after the onset of the symptoms referable to involvement of the central nervous system. A few lived for ten days to one month. Finally, two patients recovered from their acute attacks and died later with organized and canalized thrombi in their superior longitudinal sinuses.

Venereal Lymphogranuloma in Childhood.—Levy discusses the nine reported cases of venereal lymphogranuloma in children and includes observations on one additional case. Of the ten collected cases nine were in girls and one in a boy (doubtful). The ages ranged from 2 weeks to 14 years. In none was there a history of sexual contact. In none of the childhood cases was the primary lesion described. Of the nine girls, six showed inguinal adenopathy only, one had inguinal and rectal pathologic changes and only one had rectal stricture alone. The ninth patient was an infant in whose parents the disease was proved. In one case there had been an obvious cause for direct implantation of the virus into the rectum, since an enema tip used by the mother was used for the child. At least several more of the girls may have had a vaginal discharge which was not observed and the urethral route (and consequently the inguinal route) is the most likely in these cases of acquired venereal lymphogranuloma in girls. Though the course is invariably chronic the ultimate prognosis seems good, since of the ten patients six are clinically well (except

for surgical scars), one required major surgical intervention with cure, two give no record of the outcome and the tenth is the infant whose parents were affected. The therapy usually advocated is radical and complete extirpation with subsequent x-ray or quartz-lamp therapy. A characteristic early transitory vaginal discharge with urethritis accompanied by inguinal adenitis should cause one to suspect the diagnosis of venereal lymphogranuloma.

Drugs Transmitted Through Breast Milk.—If the breast milk can be used to introduce remedies of therapeutic value to the nursling, such a procedure, by proper regulation, may prove an excellent method of therapy. With this in mind Tyson and his associates carried out a study on laxatives. A questionnaire was mailed to 500 pediatricians and obstetricians; 351 answers were returned. There were 115 affirmative and 192 negative answers as to specific instances in which cathartics administered to lactating mothers were transmitted through their breast milk and produced a laxative effect or colic in the nurslings. There were fifty specific instances in which fresh fruit in season, canned fruit or foods taken by a lactating mother produced a laxative effect or colic in her nursling. There also were seventy-six positive instances in which drugs other than cathartics or laxatives administered to lactating mothers produced an untoward effect in the nurslings. After a physical examination, patients in the maternity ward of Temple University Hospital were endorsed for the study of the possible transmission of laxatives to nurslings through breast milk. From chemical analyses no trace could be found of the transmission of phenolphthalein, calomel, senna or rhubarb through breast milk. Aloin gave positive evidence of transmission through breast milk, but 87.5 per cent of the positive cases gave no clinical evidence of affecting the child. The quantities transmitted were too small for any laxative action. Cascara gave both chemical and clinical evidence of transmission. In the cases of aloin, phenolphthalein and calomel the clinical evidence in the chemically controlled series is in accordance with that found in the preliminary series. Rhubarb gave no clinical evidence whatever and it is concluded that no transmission takes place.

Kentucky Medical Journal, Bowling Green

36: 1-38 (Jan.) 1938

Acute Osteomyelitis. J. D. Hancock, Louisville.—p. 19.
Urinary Retention. E. O. Guerrant, Winchester.—p. 21.
Lobar Pneumonia. W. J. Shelton, Mayfield.—p. 25.
Role of Electrocardiogram in Diagnosis, Prognosis and Management of Cardiac Infarction. C. N. Kavanaugh, Lexington.—p. 28.
Some New Developments in Application of Plastic Surgery to Accident Cases. R. C. Pearlman, Louisville.—p. 30.
Colloidal Sulfur Therapy. R. T. Ballard, Harrodsburg.—p. 34.

Minnesota Medicine, St. Paul

21: 1-78 (Jan.) 1938

Unilateral and Bilateral Carcinoma of the Breast (Including Paget's Disease): Results Three, Five, Ten, Fifteen and Twenty Years After Operation. S. W. Harrington, Rochester.—p. 1.
New Automobiles and New Fractures. H. B. Macey, Rochester.—p. 9.
Peripheral Nerve Injuries. A. A. Zierold, Minneapolis.—p. 14.
Treatment of Burns. R. F. McGandy, Minneapolis.—p. 17.
Certain Derangements of the Knee Joint. C. C. Chatterton, St. Paul.—p. 23.
*Improved Treatment for Os Calcis Fractures. O. W. Yoerg, Minneapolis.—p. 28.
Physical Therapy in Relation to Industrial Medicine. F. H. Krusen, Rochester.—p. 30.

Treatment for Os Calcis Fractures.—Using a method evolved three years ago, Yoerg has been able to obtain improved anatomic and functional results and, in the ordinary type of os calcis fracture, men have returned to work within three months from the time of reduction. The method consists of manually disimpacting the fracture, bringing the heel down by pulling the sole of the foot, with a sudden thrust, against a firm vertical bar, and the use of an os calcis compression clamp to overcome the broadening of the heel and to replace the loosened bones to their normal or near normal position; this is followed by the application of a well molded boot cast. After reduction and the application of the cast the patient is placed in bed, with the foot elevated. He is kept in bed for three or four days or until pain has disappeared, when he is allowed to be up and about on crutches. He is discharged from the hospital, but no weight bearing is permitted. Four weeks after reduction the patient returns and the cast is removed. Roentgenograms will show that union is taking place and that it is sufficiently strong so that a cast is no longer necessary. The patient is then instructed to massage and actively and passively move the foot and ankle, particularly to evert and invert the foot to bring about a return of motion in the subastragalar joint. He continues this massage and manipulation for four weeks without weight bearing. He returns at the end of four weeks and roentgenograms taken then will show that union is firm. He is allowed to walk on the injured foot, using his crutches. In a few days or a week the crutches are discarded. In thirty-one cases there has been one failure.

New England Journal of Medicine, Boston

218: 97-142 (Jan. 20) 1938

Bronchiectasis: Physical and Psychologic Manifestations. E. D. Churchill, Boston.—p. 97.
New Method of Dealing with Funnel Chest. P. E. Truesdale, Fall River, Mass.—p. 102.
Rights and Lefts in Medical Practice. R. I. Lee, Boston.—p. 107.
Treatment of Vomiting of Early Pregnancy. D. E. Reid and H. M. Teel, Boston.—p. 109.
Low Thigh Amputation: Technic Employed in Elderly Patients, Particularly Those with Advanced Peripheral Vascular Disease or Diabetic Gangrene. G. E. Haggart and G. G. Bailey, Boston.—p. 113.
Intravenous Evipal Sodium Anesthesia in Urologic Surgery. J. E. Dunphy and J. H. Harrison, Boston.—p. 117.
*Human Autonomic Pharmacology: XVI. Benzedrine Sulfate as an Aid in Treatment of Obesity. M. F. Lesses and A. Myerson, Boston.—p. 119.

Benzedrine Sulfate in Treatment of Obesity.—Lesses and Myerson, after initial study, placed a group of seventeen unselected private patients, with a primary complaint of obesity, on a measured, unweighed diet of about 1,400 calories. No patient was urged to follow the diet or to do otherwise than obey his natural desire. All patients were observed at intervals of from seven to fourteen days. All reported symptoms were noted. Careful regulation of the dosage prevented reactions. The most satisfactory plan of treatment was to give three doses daily—a large dose (7.5 mg.) in the morning immediately on waking or rising, a moderate dose (5 mg.) at noon and a small or moderate dose (2.5 mg.) in the late afternoon. This dosage was gradually increased from week to week as the need arose, but the dosage was stopped well short of the point at which nervousness or nocturnal insomnia was produced. Ordinarily an increase of 5 mg. weekly caused no untoward symptoms. All patients were supplied with only enough tablets to last until the next visit. No patient was given a prescription for the drug or was told its name. Tolerance to the drug, so far as its effect on the appetite was concerned, did not seem to develop, for substitution of placebo tablets or omission of the drug always caused a return of increased appetite, even after months of administration. The drug was found also to be of equal benefit in cases of obesity without any obvious neurotic background, such as a case associated with narcolepsy and several cases associated with endocrine stigmas. The patients were observed over periods of from six to twenty-three weeks with a total loss of weight of from 0 to 54 pounds (24.5 Kg.).

New Jersey Medical Society Journal, Trenton

35: 1-66 (Jan.) 1938

Colloidal Thorium in Radiologic Practice. R. Pomeranz, Newark.—p. 7.
Conduct Disorders in Childhood. L. B. Hohman, Baltimore.—p. 10.
Selection of Treatment for Tuberculous Patient. J. B. Amberson Jr., New York.—p. 17.
Medical Aspects of Coma, with Particular Reference to Respiratory Disturbances. W. H. Lewis Jr., New York.—p. 23.
A Historical Note on Coronary Thrombosis. A. E. Parsonnet, Newark.—p. 27.
The Heritage of Health. W. G. Herrman, Asbury Park.—p. 33.

Public Health Reports, Washington, D. C.

53: 1-36 (Jan. 7) 1938

Studies on Chronic Brucellosis: III. Methods Used in Obtaining Cultures. Mary A. Poston.—p. 1.
Age of Gainful White and Negro Female Workers of the United States, 1920 and 1930: Studies on Age of Gainful Workers Number Five. W. M. Gafafer.—p. 4.
Study of Variations in Reports on Hospital Facilities and Their Use. J. W. Mountin, E. H. Pennell and Emily Hankla.—p. 17.

Rocky Mountain Medical Journal, Denver

35: 1-88 (Jan.) 1938

Interrelation of Hormones and Uterine Bleeding. E. C. Sage, Omaha. —p. 19.
Sulfanilamide in Treatment of Streptococcic Infections: Good Effects and Bad Effects. J. J. Waring and W. A. Rettberg, Denver.—p. 26.
Detection and Treatment of Carbon Monoxide Poisoning. R. T. Legge, Berkeley, Calif.—p. 34.
*Rocky Mountain Spotted Fever, with Reference to Recognition, Prevention and Treatment. G. E. Baker, Casper, Wyo.—p. 36.
Treatment of Osteomyelitis and Septicemia by Bacteriophage. F. H. Albee, New York.—p. 43.
The American Hospital Steps Ahead. E. A. Van Steenwyk, St. Paul. —p. 47.

Rocky Mountain Spotted Fever.—In the treatment of tick fever, Baker resorts to symptomatic and supportive measures. Bed rest with hospital care has been enforced, together with the use of a soft, high carbohydrate diet during the early stages of the illness, increased to a light diet when adequate improvement has come about. Strained fruit juices are given in abundance and enemas are used as necessary. Medication has consisted of the use of 5 grains (0.3 Gm.) of quinine sulfate, half a grain (0.03 Gm.) of codeine sulfate and 5 grains of acetylsalicylic acid every four to five hours during the acute stages of the illness, together with the use of neoarsphenamine in metaphen given intravenously. The use of neoarsphenamine dissolved in metaphen, used intravenously, is not claimed in any way to be a specific, but clinical evidence has shown that the material has value. Their therapeutic action is not understood. Neoarsphenamine, 0.3 Gm., is dissolved in 10 cc. of 1:1,000 solution of metaphen. The mixture is warmed and injected slowly into the median cubital vein, twenty minutes being taken to administer it. Blood is alternately withdrawn into the syringe and the material slowly injected until the entire amount has been given. The injections are given the first thing in the morning, the patient receiving no breakfast, at intervals of from three to five days during the acute stages of the illness. The use of the combination of the two drugs appears to affect favorably the course of tick fever. Patients show less toxemia, the eruption tends to remain discrete, renal and myocardial complications do not occur and the disease process itself is shortened. Convalescence is shorter, as a rule, and no complications have occurred. None of them had ever received prophylactic immunizations of tick vaccine.

Southern Medical Journal, Birmingham, Ala.

31: 1-126 (Jan.) 1938. Partial Index

Undulant Fever: Comparative Value of Certain Diagnostic Tests. A. E. Keller, C. Pharris and W. H. Gaub, Nashville, Tenn.—p. 1.
*Accidental Discovery of Symptomless, Nonmanifest Pulmonary Tuberculosis. C. H. Cocke, Asheville, N. C.—p. 7.
Protamine Insulin in Treatment of Juvenile Diabetes. Priscilla White, Boston.—p. 15.
Early Results in Cervix Carcinoma from Single and Divided Doses of Roentgen Radiation. A. N. Arneson, St. Louis.—p. 21.
*Sarcoidosis: Report of Case. W. B. Blanton, Richmond, Va.—p. 26.
Role of Liver Damage in Mortality of Surgical Diseases. F. F. Boyce and Elizabeth M. McFetridge, New Orleans.—p. 35.
Influence of Race on Proctology in the South. C. Rosser, Dallas, Texas. —p. 52.
The Management of Arteriosclerotic Disease of Lower Extremities. J. R. Veal, New Orleans.—p. 54.
Eye Changes in the Management of Hypertensive Toxemia of Pregnancy: A Five Year Study. A. V. Hallum, Atlanta, Ga.—p. 64.
Follow-Up Study of Thirty-One Cases of Acute Urinary Infection in Female Children. L. R. Wharton, Baltimore, and L. A. Gray, Louisville, Ky.—p. 68.
Poliomyelitis: Clinical Observations at Memphis During 1936-1937. G. J. Levy, Memphis, Tenn.—p. 71.
Cerebrospinal Meningitis in Flood Refugee Center. W. DeKleine, Washington, D. C., and W. P. Scarlett, Little Rock, Ark.—p. 75.
Study of Blood Magnesium in Allergic Individuals. A. H. Braden and A. H. Braden Jr., Houston, Texas.—p. 85.

Symptomless Pulmonary Tuberculosis.—Extensive tuberculosis, not yet manifested in symptoms, is being so frequently uncovered by roentgenography that Cocke maintains that no physical examination is complete without its use. One of the most striking paradoxes of tuberculosis is the absence of parallelism between symptoms, signs and x-ray evidence of disease. It is common to find symptoms without demonstrable physical signs but with definite x-ray evidence. There may be absence of both symptoms and signs, and yet the roentgenogram may reveal sufficiently definite (active) disease to make the diagnosis clear. Again, though more rarely, the roentgenogram may seem apparently clear, though symptoms and signs are unequivocal. This type the author assumes has a pathologic condition of such similar density to lung and other structures of the chest that it fails to register on the roentgenogram to the point of recognition. Of the ten cases that he cites only one patient admitted any appreciable loss of weight, only one complained of a cough, only four gave a history of temperature, only one gave a history of an attack of pleurisy, only one complained of increasing fatigue and mild digestive symptoms and only one at first reported sputum (but six were found to have acid rods in the sputum). With the possible exception of the young man who expectorated a little blood, there was no history in any of the patients which might seem to point expressly to tuberculosis. The roentgenogram, however, in every instance was definitely positive for tuberculosis, four cases presenting definite cavitation not demonstrable by physical examination.

Sarcoidosis.—Blanton cites a case of sarcoidosis that differs from the usual description of sarcoidosis in the following aspects: 1. The lesions of the bone, while typical of the disease in their appearance, are predominantly in the carpal and metacarpal bones, whereas in the average case the phalanges are involved more extensively. 2. The complicating arthritis, a condition under which the disease has masqueraded since the first appearance of symptoms four years ago, shows extensions of its pathologic process from bone to joint structures. 3. The microscopic appearance of the lymph node removed from the axilla shows that the nests of epithelioid cells are smaller and less prominent than those usually encountered and the enlargement of the follicles with hyperplasia of the nodes suggests earlier changes than have been observed heretofore. 4. Cutaneous lesions are absent. This uncommon circumstance emphasizes the importance of not excluding this disease from the field of general medicine, in which, by virtue of its protean manifestations, it appears to belong.

Surgery, Gynecology and Obstetrics, Chicago

66: 1-128 (Jan.) 1938

Hurthle Cell Tumor of Thyroid Gland. A. O. Wilensky and P. A. Kaufman, New York.—p. 1.
Congenital Anomalies of Rectum and Anus. J. K. Berman, Indianapolis. —p. 11.
*Use of Os Purum in Bone Implantations, with Especial Reference to Its Use in Tuberculous Bone and Joint Lesions. S. Orell, Stockholm, Sweden.—p. 23.
Diabetes and Pregnancy. W. W. Herrick and A. J. B. Tillman, New York.—p. 37.
Upper Pelvic Floor and Its Importance in Total Abdominal Hysterectomy. Lilian K. P. Farrar, New York.—p. 44.
Biologic Surgery in Tuberculous Patients. C. R. Lavalle, Buenos Aires, Argentina.—p. 55.
*Thrombophlebitis of Appendical Vein Complicating Acute Appendicitis. S. Z. Hawkes, Newark, N. J.—p. 62.
Conservative Treatment of Gallbladder Disease. H. E. Mock, C. F. G. Brown and R. E. Dolkart, Chicago.—p. 79.
Interposition Operation with Sterilization. F. I. Harris, San Francisco. —p. 88.
Hallux Valgus. W. I. Galland and H. Jordan, New York.—p. 95.
Instrumental Dilatation of Papilla of Vater: Experimental and Clinical Observations. R. Zollinger, C. D. Branch and O. T. Bailey, Boston. —p. 100.
Conduction Analgesia in Anorectal Surgery. H. E. Bacon, Philadelphia. —p. 105.
Treatment of Fistulas of Small Intestine. J. B. Hartzell, Detroit.—p. 108.
Uterus Bicornis Duplex Associated with Infection Due to Micro-Aerophilic Hemolytic Streptococcus. E. B. Self and F. L. Meleney, New York.—p. 117.

Bone Implantations.—In implantation of bone in the skeleton, one should use bone in such form and manner that the skeletal connective tissue in it can quickly revive and that the living skeletal connective tissue in the compact bone in the bed of the implant may grow into the canal system of the implant as easily and as quickly as possible. To fulfil the first qualification, fresh autoplastic bone is ideal; to fulfil the second, bone which Orell has called "os purum," and which is prepared in a special manner, is nearest ideal. Ordinary bone is freed as completely as possible of connective tissue, fat and protein foreign to the host, and the calcified substance made as clean as possible without injuring its mechanical strength. The method of preparation consists chiefly of the removal of the blood proteins by soaking in saline solution, the connective

tissue by soaking in warm potassium hydroxide and the fat by soaking in acetone. The author has used the implantation of os purum in forty-nine cases to replace bone. It has been used to fill up the bone defects which result from operation, to lessen the chance of producing deformities and to fix the parts of the skeleton in proper relation to one another in various ways often after replacing, reshaping or changing their position. Many of the patients with implants of os purum have now been observed for four or five years. The wounds have, as a rule, healed without complications and the implants have shown sufficient strength for their mechanical task until they have gradually been rebuilt and replaced by new bone. Implantation of os purum should be preferably done in cases of bone tuberculosis when the disease is in a quiescent stage and when the lesions have shown some tendency toward localization. Even in many cases of joint resection in more active forms of tuberculosis os purum may give a good result. It is only in cases in which fistulas have formed or in cases in which the overlying skin has been rendered thin and unhealthy by secondary infection or abscess formation that the implant is sometimes extruded. In using os purum, an especially careful aseptic technic is demanded. A good clinical result from the implantation of os purum may be expected only when skeletal connective tissue is present in the bed of implantation. In implants into the epiphysis, large surfaces of cancellous bone must lie against the os purum; in implants into the diaphysis, living periosteum as well as compact bone must surround it.

Thrombophlebitis of Appendical Vein.—Hawkes declares that one of the factors which contribute to the high mortality rate of appendicitis is failure, in some cases, to recognize thrombophlebitis of the appendical vein. This complication so alters the diagnostic, pathologic, prognostic and therapeutic features that there may be justification for placing appendicitis, thus complicated, in a category of its own. A survey of this type of appendicitis is attempted, together with the operative treatment thus far practiced. The occurrence of a chill and typical symptoms of acute appendicitis point to a complicating thrombophlebitis of the appendical vein. The treatment consists in ligation of the ileocolic vein above the thrombus before appendectomy is performed. Unless the condition is treated early and the ileocolic vein ligated, emboli may occur, causing either pylephlebitis or liver abscesses. Early recognition and proper treatment of this type of appendicitis may contribute to lowering the mortality rate of appendicitis as a whole.

United States Naval Med. Bulletin, Washington, D. C.

36: 1-162 (Jan.) 1938

Diabetes and Protamine Insulin. E. P. Joslin.—p. 1.
Compressed Air Illness. C. W. Shilling.—p. 9.
Treatment of Hay Fever with Alum Precipitated Pollen Extract. R. F. Sledge.—p. 18.
Malaria. W. H. Michael.—p. 29.
Barbiturate Poisoning: Review with Report of Two Cases. F. L. McDaniel and R. A. Bell.—p. 32.
Carboxide Poisoning. J. D. Blackwood Jr. and E. B. Erskine.—p. 44.
Sulfanilamide Therapy of Gonorrhea. R. H. Snowden and R. A. Bell. —p. 45.
*Sulfanilamide Treatment of Ludwig's Angina. J. E. Fulghum.—p. 58.
Psychosis Precipitated by Sulfanilamide. B. W. Hogan and P. J. McNamara.—p. 60.
Sulfanilamide Poisoning: Report of Fatal Case. J. T. O'Connell.—p. 61.
Results of Sulfanilamide Therapy of Gonorrhea. E. R. Hering.—p. 63.
Chondrodystrophy Fetalis. W. S. Sargent.—p. 67.
The Cancer Problem in the United States Navy. O. B. Spalding.—p. 74.
Carcinoma of Lung. I. J. Warmolts.—p. 79.
Bronchogenic Carcinoma: Metastases to Heart and Pituitary: Case Report. I. L. Norman and W. M. Silliphant.—p. 89.

Sulfanilamide in Treatment of Ludwig's Angina.—Fulghum administered sulfanilamide intramuscularly to a child, aged 3 years, who had Ludwig's angina resulting from streptococci entering from a lesion on the chin. The progress of the disease was arrested and there was a gradual regression of swelling without formation of pus and with rapid return to normal as compared to the usual surgical treatment. Although only one case is reported, the author feels that sulfanilamide is a valuable drug in the treatment of Ludwig's angina due to streptococci and that by its use the mortality rate of Ludwig's angina will be decreased greatly.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Dermatology and Syphilis, London

50: 1-58 (Jan.) 1938

Psychologic Aspects of Skin Diseases. R. D. Gillespie.—p. 1.
Cutaneous and Subcutaneous Leishmaniasis. R. B. Evans.—p. 17.
Pseudo-Atrophoderma Colli. L. Goldman and E. B. Tauber.—p. 22.
Dupuytren's Contraction, Camptodactylia and Knuckle Pads: Note. F. P. Weber.—p. 26.

British Journal of Ophthalmology, London

22: 1-64 (Jan.) 1938

Congenital Vascular Veils in Vitreous. Ida Mann and A. Macrae. —p. 1.
Intra-Ocular Neuroma (von Recklinghausen's Disease) of Left Optic Nerve Head: Case. H. B. Stallard.—p. 11.
Significance of Heredity in Ophthalmology: Preliminary Survey of Hereditary Eye Diseases in Tasmania. J. B. Hamilton.—p. 19.
Use of Contact Glass for Cosmetic Purpose. S. K. Mukerjee.—p. 43.
Stenopeic Spectacles. A. L. Young.—p. 45.

British Medical Journal, London

2: 1261-1310 (Dec. 25) 1937

Tuberculosis in Hospital Workers. P. W. Edwards.—p. 1261.
Vinyl Ether as an Anesthetic Agent. V. Goldman.—p. 1265.
Anesthesia in Minor Surgery. J. H. T. Challis.—p. 1269.
*Visceral Pain. J. Morley.—p. 1270.
Brucellosis in Man and Animals in Staffordshire: Laboratory Observations. J. Menton.—p. 1273.

Visceral Pain.—Morley limits his remarks to the mechanism of visceral pain and for the most part with pain originating in the gastro-intestinal tract. The one stimulus adequate to produce direct visceral pain in the gastro-intestinal tract appears to be tension on the afferent nerves in its muscular coats, and this tension is usually caused by spasmodic and exaggerated peristaltic contraction. The sensitive mesentery is often involved in such lesions as strangulation and volvulus, and this causes a combination of visceral and somatic pain that is not easy to unravel. The nerves of the sensitive parietal peritoneum must receive the stimulus that gives rise to the pain and tenderness in the superficial parts of the abdominal wall and to the associated reflex muscular rigidity. The process is described as peritoneocutaneous radiation and a peritoneomuscular reflex. An appreciation of this peritoneocutaneous radiation is essential for any true understanding of abdominal pain, and the mechanism is best illustrated by stimulation of the phrenic nerve terminals below the diaphragm. When the undersurface of the central portion of the diaphragm receives a painful stimulus, immediate pain is felt in the region of the descending branches of the third and fourth cervical nerves supplying the skin of the supra-acromial region. Infiltration with procaine hydrochloride of the area of skin supplied by the third, fourth and fifth cervical nerves either abolishes or greatly modifies the referred pain caused by stimulation of the diaphragm. A study of phrenic pain leads to the conclusion that a precisely similar peritoneocutaneous radiation occurs in the superficial nerves of the anterior abdominal wall when the underlying parietal peritoneum receives a painful stimulus from an inflamed viscus or inflammatory exudate. The localizing pain in acute appendicitis or acute cholecystitis is greatly modified or completely abolished by inducing local anesthesia by subcutaneous infiltration of the area in which the pain is felt. Whatever the ultimate truth may be as to the mechanism of referred pain in angina, the author contends that it differs fundamentally from the mechanism of pain in the gastro-intestinal tract, in which there certainly is a dual mechanism. On the one hand, one sees true visceral pain as part of a defense against the threat of obstruction. It is primitive in the scale of evolution, is in no sense referred to the superficial somatic nerves and is imperfectly and vaguely localized. On the other hand, one finds referred pain, the stimulus for which arises not from the visceral afferent nerves at all but from the somatic nerves of the parietal peritoneum. It has been evolved as a protection against bacterial infection of the peritoneum, either by penetrating wounds from without or by perforation of the intestine within. It is later in the scale of evolution and produces a radiation of pain to the superficial somatic nerves and a reflex protective rigidity of the overlying muscles, both of which are localized accurately.

V 1
193

Edinburgh Medical Journal

45: 1-72 (Jan.) 1938

Chronic Nutritional Hypochromic Anemia. L. S. P. Davidson and H. W. Fullerton.—p. 1.

Clinical Recollections and Reflections: XX. Some Observations on Notifiable Streptococcic Infections. W. T. Benson.—p. 24.

Debatable Tumors in Human and Animal Pathology: III. Seminoma. J. R. M. Innes, W. F. Harvey and E. K. Dawson.—p. 36.

Neuropsychologic Basis of Conduct Disorder. R. G. Gordon.—p. 43.

Glasgow Medical Journal

10: 245-292 (Dec.) 1937

Optic Neuritis (Retrobulbar and Papillary). L. Paton.—p. 245.

Journal of Hygiene, London

38: 1-128 (Jan.) 1938

Investigation of Factors Governing Potato Starch Refection in Rats. P. M. Kon, S. K. Kon and A. T. R. Mattick.—p. 1.

Experiment on Nutritive Value of Winter Produced "Summer" Milk. J. C. Drummond, Eleanor Singer, S. J. Watson, W. S. Ferguson and M. S. Bartlett.—p. 25.

Influence of Growing Family on Diet in Urban and Rural Districts. F. Brockington.—p. 40.

*Mechanism of Malaria Transmission in the Province of North Holland. N. H. Swellengrebel, A. de Buck and H. Kraan.—p. 62.

Incidence of Organisms of Salmonella Group in Wild Rats and Mice in Liverpool. A. M. Khalil.—p. 75.

Disease Resembling Distemper Epidemic Among Ferrets. E. T. C. Spooner.—p. 79.

Investigation into Cancer Mortality Among Males in Certain Sheffield Trades. H. M. Turner and H. G. Grace.—p. 90.

*Intradermal Test in Whooping Cough: Review, with Study of 1,300 Cases. A. R. Thompson.—p. 104.

Keeping Qualities of Vaccine Lymph. G. G. Butler.—p. 120.

Mechanism of Malaria Transmission.—Swellengrebel and his co-workers state that the rate of malarial infection in nature is more than a hundred times higher in Anopheles maculipennis atroparvus than in Anopheles maculipennis messeae. The periodicity of anopheline malaria is the effect of the periodically recurring intermissions in the fertility of Anopheles maculipennis atroparvus, associated with continued blood feeding. These intermissions occur independently of temperature. Anopheles can become infected at least as late as October 7. An infection acquired at that time takes no more than three weeks to reach the salivary glands. Winter contributes to the shaping of the epidemiology of malaria in Holland by causing the sporozoites to degenerate. Anopheles spread the malaria parasites from man to man and from house to house in the autumn. Man keeps them alive till the next transmitting season. Man spreads malaria from village to village. Anopheline malaria dies out in a house by the deterioration of the human parasite reservoir or by the lack of Anopheles, resulting from the removal of appropriate places for Anopheles to hide in. But it can also become extinct because human parasite carriers lose their infectivity before they get rid of their parasites. The failure of infected Anopheles, staying in a house, to cause malaria in the human inmates of that house during the next year is due to a partial immunity or to an unusually long period of incubation of the human host. The incidence of human malaria is highest near the foci of anopheline malaria of the preceding year. The scattered cases of malaria (one-patient houses) do not all conform to this rule. Their distribution suggests that a certain number (less than one fifth) of the malaria houses are infected by Anopheles carrying sporozoites during the period of their sexual activity in the second half of July and the first half of August.

Intradermal Test in Whooping Cough.—The conflicting views of investigators prompted Thompson to observe the intradermal reaction in a comprehensive series of cases and suggested that, as far as Haemophilus pertussis was concerned, any cutaneous response would be allergic in nature, as distinct from the toxin-antitoxin reactions elaborated in the Schick and Dick tests. Comparative tests were therefore performed on a total of 1,300 subjects, 1,182 of whom were less than 10 years of age and 300 of whom were suffering from pertussis. The observations do not support the claim that the intradermal response to Sauer's vaccine in the strength commonly employed (10,000 million organisms per cubic centimeter) is of value either in demonstrating immunity to whooping cough or in its early diagnosis. The bacterial content of this vaccine appears to be too high for purposes of skin testing, giving rise to inflammatory lesions of a nonspecific character rather than to allergic reactions of specific value. These reactions are less apparent when the vaccine is employed in a diluted form. The intradermal response to pertussis endotoxin, on the other hand, though not invariably consisting of a clear-cut reaction, is more consistent with the development of the allergic state toward Haemophilus pertussis, reactions presumably of this nature being present in the skin of approximately 85 per cent of children with a past history of whooping cough. Similar reactions, however, can be elicited in the skin of about 30 per cent of the subjects with no history of the disease; but in view of the fact that, unlike the more invasive virus diseases, many persons never develop whooping cough in spite of almost certain exposure when young, it is suggested that latent immunization or recent contact with the causative organism might account for this phenomenon. The onset of bacterial hypersensitiveness, as judged by the pertussis endotoxin test, appears about the tenth day of whooping cough and becomes heightened during the subsequent course of the disease. Ultimately this cutaneous allergy undergoes a regression, which, however, is not always complete. For this reason the pertussis endotoxin test would appear to be of some value in assessing the immune state of the individual, and also as a diagnostic reaction in early, atypical or late cases of whooping cough in which bacteriologic observations by the cough plate method have proved disappointing.

Journal of Laryngology and Otology, London

52: 803-890 (Dec.) 1937

*Subglottic Cancer of Larynx. St. Clair Thomson.—p. 803.

Bilateral Ossification of Stylohyoid Ligament Combined with Cervical Exostoses. J. B. Cavenaugh.—p. 817.

Subglottic Cancer of Larynx.—Sixteen years ago St. Clair Thomson, when studying the most usual site for intrinsic cancer of the larynx, found that in fifty consecutive cases there were thirteen in which the subglottic region was involved. The usual intrinsic cancer originates on the upper surface or on the free margin of a cord. A subglottic neoplasm may also take its origin on the inner or lower surface of the cord, but below its free edge, which then remains intact until the growth extends up to it from below. Until this occurs the voice may not be affected and the symptoms may be trifling. The typical subglottic cancer arises in the area below and distinct from the cord, sometimes as low as the cricoid ring. As the neoplasm grows it tends to extend upward until, when advanced, it appears on the edge of the cord. But a subglottic growth may even run its course without ever extending to a cord. In the subglottic group, alteration of voice is not the first or an early noticeable symptom. The patient may first complain of occasional "colds in the throat" and at times may feel the voice veiled and find difficulty in shifting any catarrh from the larynx. The gradual onset of slight dyspnea and stridor on exertion—two indications much neglected both by the public and by the profession—may first bring the case to a laryngologist, who may fail to detect anything serious in the early stages or may notice only occasional or even variable paresis of one cord. Many patients do not seek advice until the neoplasm has reached the edge of the cord and begins to cause hoarseness. When a cord is clear or only congested, or when the margin is simply serrated at one point and particularly when the movement is at all impaired, careful inspection may reveal a subglottic growth. A subglottic cancer may occur in early life and even when grown to a considerable size the correct diagnosis may be overlooked by a whole group of experts. When an unsuspected subglottic growth extends upward until it reaches the free edge of the cord, it may produce a "mouse-nibbled" ulceration and its first appearance may simulate a tuberculous lesion. A biopsy would be of help in these cases, if a satisfactory specimen could be obtained. Recent improvements in x-ray technic give promise of being helpful in determining the full extent of a subglottic cancer. The prognosis in all cases of subglottic cancer is much less hopeful than in intrinsic cases limited to the free edge or surface of the cord. Of the thirteen patients with subglottic disease seven have died of recurrence. Again, impaired mobility of a cord is encountered more frequently in subglottic cases and is of evil augury. Thus, of twenty-seven patients with a mobile cord, twenty-one were alive and free from local recurrence three years later, while

of seventeen with impaired movement only seven were alive and free from recurrence. In the thirteen cases of subglottic cancer the cord was fixed in no less than six cases. It is difficult to decide when subglottic cases might be adequately dealt with through a laryngofissure, and when a more extensive operation (generally a complete laryngectomy) is necessary. If the subglottic growth has not reached the arytenoid region or spread as low as the cricoid cartilage and has not invaded the anterior commissure or crossed to the other side, removal by the laryngofissure route can be quite successful in securing a lasting cure, even if impaired mobility of the cord is noted. Even fixation of the cord, although it diminishes, does not destroy the possibility of lasting cure by a laryngofissure. Although not nearly so promising, even a bilateral subglottic cancer, if it has not invaded the actual anterior commissure, can be successfully treated through a laryngofissure. Invasion of the anterior commissure itself often means spread of the disease through the cricothyroid membrane into the soft tissues of the neck. In such cases the probability of a successful result, even by a complete laryngectomy, is diminished.

Journal of Mental Science, London

83: 609-752 (Nov.) 1937

*Convulsion Therapy in Schizophrenia. A. Kennedy.—p. 609.
Unusual Complication of Insulin Shock (Hypoglycemic) Therapy. C. B. Molony and M. S. Honan.—p. 630.
Value of Continuous Narcosis in Treatment of Mental Disorder. H. A. Palmer.—p. 636.
Epileptic Reactions: Attempt at Classification. A. Guirdham.—p. 679.
Treatment of Epilepsy with Psychosis by Prominal. D. E. Sands.—703.
Familial Psychoses Associated with Endocrine Disorder. T. A. Munro.—p. 707.
Profound Dissociation of Personality: Case. C. L. Copeland and E. H. Kitching.—p. 719.

Convulsion Therapy in Schizophrenia.—Kennedy gives an account of his experience of convulsion treatment of schizophrenia, reviews the literature and reports three cases recently treated at West Park Hospital. More than 1,000 cases have now been treated at various hospitals in Europe, and the mortality and remission rates, especially in the catatonic type of case, compare favorably with the insulin shock treatment. The permanence of the remissions produced by this method cannot as yet be assessed. Discussion as to the type of schizophrenia which reacts most favorably to convulsion therapy has been ambiguous, owing to the differing ways of describing clinical syndromes, but there is little doubt that in the classification of Kraepelin the catatonic form reacts best and the paranoid is least affected, in contrast to the results of insulin treatment. Recently, while giving insulin shock treatment to six patients, Molony and Honan found that one patient on the twenty-second day of treatment did not awake from the hypoglycemic coma on being given food. Intravenous dextrose and epinephrine also failed to revive her. Blood and spinal fluid sugars were then found to be excessive and antidiabetic treatment (including insulin) was administered with success.

Lancet, London

1: 1-64 (Jan. 1) 1938

Surgical Treatment of Angina Pectoris and Allied Conditions. D. T. Davies, H. E. Mansell and L. O'Shaughnessy, with cooperation of Dawson.—p. 1.
*New Syndrome Apparently Due to Overactivity of Posterior Pituitary. E. I. Jones.—p. 11.
*Clinical Hyperfunction of Posterior Lobe of Pituitary: Suggested by a Pressor and Antidiuretic Substance Obtained from Urine. R. L. Noble, H. Rinderknecht and P. C. Williams.—p. 13.
*Electrosurgical Obliteration of Gallbladder Without Drainage: Report of 342 Cases. M. Thorek.—p. 15.
*Vitamin C Output in Diet Treatment of Rheumatoid Arthritis. D. C. Hare and E. C. P. Williams.—p. 20.
Prevalence of Sonne Enteritis. L. H. D. Thornton and E. M. Darmady.—p. 25.

Overactivity of Posterior Pituitary.—For eight months Jones has observed a patient who presented a combination of hypertension, hyperchromic anemia, achlorhydria and abnormal carbohydrate tolerance. An extract of the patient's urine contained a substance or substances which had the actions of solution of posterior pituitary and the clinical observations suggest that there is hyperfunction of the posterior lobe of the pituitary. The fact that, as his condition improved, the amount of pituitary-like substance excreted in the urine diminished indicates that the hyperfunction is either an isolated occurrence or is possibly cyclic in nature. Continued observation of the patient will settle this point. The syndrome described is thought to be new to clinical medicine, but the diseases that are known to affect the anterior lobe of the pituitary and other ductless glands lead one to believe that the hyperfunction of the posterior pituitary is at least theoretically possible.

Hyperfunction of Posterior Lobe of Pituitary.—The similarity between the condition of the patient in the preceding abstract and that which could be produced in animals suggested to Noble and his collaborators that it would be of interest to determine whether the vasopressive principle could be obtained from the patient's blood or urine. Specimens of blood and urine were collected in May and July. An extract containing pressor and antidiuretic activity has been obtained from the urine, suggesting hyperfunction of the posterior pituitary. The effects of this extract are similar to those produced by the pressor principle of pituitary preparations.

Electrosurgical Obliteration of Gallbladder.—Thorek felt that, if a dry, nonleaking surface could be substituted for the discharging cavity represented by the bed of the gallbladder resulting from classic cholecystectomy, it would be an important step. Experimental studies on dogs and monkeys proved that this can be accomplished by proper electrocoagulation. The tendency of electrocoagulated surfaces to become agglutinated with serous surfaces requires putting into service the falciform ligament. So far (August 1937) 342 operations have been performed by this method in cases of gallbladder disease including gangrene, empyema and sclerosis. There were three deaths in the series. One patient succumbed to an undiagnosed chronic subdiaphragmatic abscess some time after operation. Another patient died from massive bilateral pulmonary collapse and the third from pneumonia about three weeks after the operation. Failures and fatalities in classic cholecystectomy are often due to bile leakage, as a result of an inability to obliterate and cover the bed of the gallbladder, and drains invite bile seepage. With this method a prerequisite to satisfactory results is a patent common duct. An occluded cystic duct from any cause is an indication for this operation. The operation effectually accomplishes destruction of the entire thickness of the wall of the gallbladder and, if indicated, also the bed of the gallbladder. The surgeon has under control the degree of penetration he wishes to accomplish. The ligamentum falciforme hepatis is used as a free graft; its serous structure covers sutured or raw surfaces to great advantage, thus reinforcing and protecting the areas concerned against seepage and safeguarding the processes of repair. Electrocoagulated areas of intra-abdominal organs tend to heal by encapsulation. They do not interfere with wound healing. Therefore drainage is not only undesirable but is distinctly deleterious. Electrosurgical obliteration of the gallbladder exacts careful technic and meticulous attention to detail.

Vitamin C Output in Diet Treatment of Rheumatoid Arthritis.—During the last eighteen months Hare and Williams have been studying the effects of a raw vegetable and fruit diet in six cases of rheumatoid arthritis with a view to determining the effective factor in the diet. In this the two most striking variants from an ordinary mixed diet were the abnormally high vitamin C and the abnormally low sodium chloride content. One patient could not be kept strictly to the diet. The other five patients showed definite clinical improvement.

Medical Journal of Australia, Sydney

2: 1019-1060 (Dec. 11) 1937

Peptic Ulcer: Analysis of 218 Cases Studied at Autopsy. R. J. Wright-Smith.—p. 1027.
Bleeding Peptic Ulcer. I. J. Wood.—p. 1031.
Artificial Hatching of Taenia Saginata Ova. W. J. Penfold, H. B. Penfold and Mary Phillips.—p. 1039.

2: 1061-1106 (Dec. 18) 1937

*Substances Controlling Growth of Implanted Tumors. W. Moppett.—p. 1065.
Acrocyanosis. C. G. Lambie and S. M. Morson.—p. 1070.

Substances Controlling Growth of Implanted Tumors.—Moppett agrees with the conclusions of other workers that extracts of the anterior pituitary containing both growth and gonadotropic hormones appear to stimulate the growth of an

implanted tumor and that thyroxine may in certain circumstances retard the growth of implanted tumors. One can regard a tumor as in some respects a dedifferentiation. In the early embryo differentiation is believed to result, partly at any rate, from certain definite chemical molecules termed organizers. In certain amphibian embryos a second neural canal can be brought about by certain ether soluble substances which are probably related to cholesterol and to the cancer producing molecules. One would expect an organizer to retard tumor growth by causing differentiation of the tumor cells, and thyroxine may be considered in this class of substance in virtue of its action on amphibian metamorphosis. There is thus a prospect of controlling cancer growth by administration of organizers. One would not expect success in every case with a given substance, since organizer action depends on "competence" of a given tissue to respond. Nevertheless, if thyroxamine or a more potent derivative, or some of the cholesterol derivatives, would control any recognizable tumor, a new era in cancer treatment would be introduced.

Practitioner, London

139: 633-736 (Dec.) 1937

Development of Chemotherapy for Bacterial Diseases. H. Hoerlein.—p. 635.
*Assessment of Efficiency of Chemotherapeutic Substances. L. E. H. Whitby.—p. 650.
Use of Antistreptococcus Preparations in General Practice. A. H. Douthwaite.—p. 661.
Use of Antistreptococcus Preparations in Obstetrics. A. C. Bell.—p. 673.
Nomenclature and Dosage of New Antistreptococcus Preparations. W. K. Fitch.—p. 680.
Acute Pulmonary Edema: Its Pathogenesis and Treatment. M. Campbell.—p. 689.
Environment in Treatment of Psychoneuroses. Grace Nicolle.—p. 696.
Stammering Habit: Correction Through Speech Reeducation. H. St. J. Rumsey.—p. 707.
Diet in Health and Disease: VI. Diet in Gastric Diseases. M. E. Shaw.—p. 715.

Efficiency of Chemotherapeutic Substances.—Whitby shows what sound evidence there is for believing the sulfanilamide compounds to be effective, how such evidence has been collected and suggests how further evidence may be accumulated. The investigation of hemolytic streptococcus infections in mice has presented relatively few difficulties. Results have been consistent. The meningococcus has presented more difficulty, but the results have been sufficiently convincing to warrant the use of sulfanilamide in the human subject. With the pneumococcus the experiments have been irregular and unconvincing; there is no sound experimental work to suggest that sulfanilamide has any marked action in pneumococcic infections; and this despite the fact that mice are readily susceptible to infection so that a clear-cut result, a reduction in mortality rate, could be obtained if sulfanilamide were really effective. Bacillus coli and Streptococcus viridans cannot be satisfactorily investigated in an experimental animal. There is a considerable breach to be filled between proving the efficiency of a drug in an animal and the use of the same drug in the human subject. The ideal assessment is made with a group of treated patients compared with an equal group of untreated controls. Were one of the medical journals to undertake the proper collation of information from general practitioners concerning their experience with definite remedies, valuable deductions could be made. The reports concerning puerperal sepsis have been models of discretion. It is justifiable, however, to use it whenever there is sound reason to anticipate puerperal sepsis; for example, in any case in which delivery is effected with much instrumental intervention or in suggestive circumstances. The treatment of erysipelas with sulfanilamide has been uniformly successful. As streptococcic meningitis has ordinarily a mortality of about 100 per cent, one cannot but be impressed with the reports of successful treatment in individual cases. Sulfanilamide appears rapidly in the cerebrospinal fluid and, experimentally, the drug is known to have an effect on meningococci. The value of sulfanilamide in gonorrhea is in the process of being properly assessed. Experimentally the drug is apparently effective against the gonococcus and there is every reason to suppose that it will benefit gonorrhea because the compound is not only excreted in the urine but is also, more important, present in blood serum and tissue fluids. The use of sulfanilamide in Bacillus coli infections of the urinary tract was first advocated by Huber (1936), who obtained striking results in the pyelitis of children. There is good evidence that the drug is effective in these infections. It has not yet been shown whether or not the relapse rate is less after sulfanilamide than after other modern forms of treatment. Clinical successes have been claimed for the treatment of pneumococcic infections as well as gas gangrene. There is not yet sufficient evidence to show whether or not these claims are justified. The drug will tend to be discredited if used irrationally. The therapy is not without danger. Possible complications now include sulfhemoglobinemia and methemoglobinemia, as well as acute hemolytic anemia, agranulocytosis, drug fever, cutaneous eruptions, including purpura, and optic neuritis. Because the drug has toxic properties it is preferable to prescribe it for those who are at rest in bed and who are under daily observation, not for those who are ambulant.

Archives de Médecine des Enfants, Paris

41: 1-64 (Jan.) 1938

Levulosuria in Child: Study of Rare Disorder of Carbohydrate Metabolism. G. Paisseau, J. Ferroir and A. Mangeot.—p. 5.
Treatment of Interstitial Keratitis in Course of Congenital Syphilis. E. Lesné and D. Ronget.—p. 11.
*Time of Appearance of Meningitis in Course of Tuberculous Infection. P. Nobécourt and S.-B. Briskas.—p. 17.
Perihilar and Periscissural Images with Chronic Nonbacillary Evolution in Children. F. Tissot.—p. 26.
*Administration of Globulins of Placenta in Some Infectious Diseases of Children. O. Felsenfeld.—p. 30.

Meningitis in Course of Tuberculous Infection.—Nobécourt and Briskas investigated the time of appearance of meningitis in the course of tuberculous infection in children up to the age of 15 years. The material on which their investigations were made is the following: 1. There were 344 cases of tuberculous meningitis that were observed during the fifteen years between 1921 and 1935 inclusive, among a total number of 13,331 children, who were admitted to the children's clinic during that time; this represents an incidence of 2.5 per cent. 2. There were twenty-four cases of tuberculous meningitis observed during the year 1936 among 1,645 children, which represents an incidence of 1.4 per cent. The total of 368 cases of tuberculous meningitis observed among 14,976 hospitalized children represents an incidence of 2.4 per cent. The authors first take up the twenty-four cases that were observed during 1936. Classification according to the months in which the tuberculous meningitis developed reveals that the frequency is greatest during April, July, August and September. The same frequency was observed from 1921 to 1935. In taking up the time of appearance of the tuberculous infection, the authors show that this encounters considerable difficulties, particularly in older children. They cite several case histories. The first one reported concerns a nursling who, at 7 months, gave negative cutaneous reactions for tuberculosis and at 10 months the nursling died as the result of tuberculous meningitis. In the second child whose history is reported, the interval between the last negative cutaneous reaction and the appearance of the tuberculous meningitis was eight months. The authors further present an analysis of the time of appearance of the tuberculous infection in twenty-seven nurslings aged from 2 to 10 months. In twenty of these the meningitis appeared from one to three months and in seven from three to six months after the tuberculous contact. In the last part of their discussion the authors present a review of the literature on this subject. On the basis of this review and of their own observations they conclude that the interval between the beginning of the tuberculous infection and the clinical manifestations of the tuberculous meningitis varies between three and six weeks on the one hand and between three and six months on the other hand. As a rule the meningitis appears during the primary phases of the tuberculous infection; it is a manifestation of the primary-secondary period. Rarely, tuberculous meningitis develops after a more or less old form of the tuberculous infection if the latter has caused lesions in various organs. Occasionally, tuberculous meningitis develops in children in whom the first infection is apparently cured and is due either to a reactivation or to a new infection.

Use of Globulins of Placenta in Infectious Diseases.—Felsenfeld points out that, although convalescent serum can be used with success in a number of diseases, the supply is not always sufficient. Therefore the use of serum of the placenta

110
938

for the prophylaxis and treatment of infectious diseases was favorably received. The author describes the protective measures employed against contagious diseases in the Institute for Tuberculous Children, with which he is connected. He points out that the globulins of the placenta, administered as soon as possible and immediately after contact with the agent of infection, protect a large percentage of children against measles and scarlet fever but are not efficacious against rubella. In the therapy of measles, scarlet fever and epidemic parotitis, the immunizing globulins produce favorable results.

Presse Médicale, Paris

46: 153-168 (Jan. 29) 1938

*Roentgen Therapy of Second Lumbar Sympathetic Ganglion in Coxarthritis. Duhem, Moro and Montmignaut.—p. 153.
Cardiovascular Tonics Used in Urgent Cases. P. Oury, H. Besson and H. Bouchara.—p. 154.
Evolutive Phases of Pulmonary Tuberculosis. M. Jaquerod.—p. 157.

Roentgen Therapy of Sympathetic Ganglion in Coxarthritis.—Duhem and his associates point out that many authors have recommended the application of roentgen rays to the diseased joints. It was found that these roentgenologically visible lesions were not influenced by the irradiations and yet the joint became more supple and the pains diminished or disappeared. The authors suggest that the sympathetic probably plays an important part in the genesis of the pains that accompany coxarthritis. They direct attention to Leriche's work on ramisectomy, ganglionectomy and sympathectomy as well as to the method that employs anesthetic infiltration of the sympathetic. The authors had the idea to employ, instead of this anesthetic infiltration, roentgen irradiation of the second lumbar ganglion in patients who had arthritis of the hip. They apply the rays to the spinal process of the second lumbar vertebra. The voltage employed is from 180 to 200 kilovolts. The intensity is 3 milliamperes; the filter consists of 0.5 mm. of a heavy metal (copper for instance) and 2 mm. of aluminum. The focal distance is 40 cm. The dosage must be sufficient, without being excessive. The authors usually employ 150 roentgens at each session, two of which are given each week. The total number of irradiations is generally six, so that 900 roentgens is applied in all. The authors employed the treatment in twenty-five cases. In a disorder as capricious as chronic arthritis of the hip it is difficult to estimate the efficacy of a treatment. Nevertheless, on the basis of results obtained with the roentgen irradiation of the second lumbar sympathetic ganglion they conclude that the treatment is without danger and that it reduces the pain and improves the walk of patients with coxarthritis. In four of the cases in which this treatment was given, amelioration was noticeable after the second or third irradiation, in six other cases after the fourth irradiation, in eight others after the sixth irradiation, and in the other cases the improvement did not become noticeable until two weeks after the irradiations, but the treatment never showed itself inefficacious. As yet they are unable to say whether the improvement will be lasting. In some cases the treatments had to be resumed at the end of a month. Moreover, a modification of the technic may be advisable.

Arch. p. 1. Stud. d. Fisiopat. e Clin. d. Ric., Siena

5: 333-412 (Sept.-Oct.) 1937

*Polypeptides in Blood in Typhoid. G. Rettanni.—p. 333.
Hemoglobin in Chemical System Regulating the Reactions of Blood. L. Antognetti.—p. 357.
Pathogenesis of Obesity in Relation to Secreting Activity of Hypophysis. L. Antognetti and D. Scopinaro.—p. 373.
*Azotemia from Administration of Food Proteins. M. Bassi.—p. 393.

Polypeptides in Blood in Typhoid.—Rettanni followed the behavior of the polypeptides in the blood of twenty-four patients who were suffering from typhoid. He found that they increase during the first week of the disease, reach the highest values in the second week, diminish by the third week and return to normal during convalescence. The index of cleavage (deamination) of the peptides, which shows dysfunction of the liver, parallels the variations of polypeptidemia. The increased amount of polypeptides in the blood, which is induced by administering 40 Gm. of peptone to the patients in the peak of the disease, lasts longer than in normal persons. The index of cleavage of peptides is also more prolonged after the test in patients with typhoid than in normal persons. According to the author the increase of polypeptides in the blood, which is proportional to the seriousness of the disease, is due mainly to a dysfunction of the liver in deaminizing peptides. The dysfunction of the liver is also proportional to the seriousness of typhoid. An increased disintegration of proteins in the blood by fever is a secondary factor. The disturbances of the nervous system and of the cardiovascular apparatus in the course of the disease are caused by a double intoxication of the structures by polypeptides and typhoid toxins.

Azotemia from Administration of Food Proteins.—Bassi found that the administration of 60 Gm. of food proteins increases azotemia slightly in normal persons, moderately in patients with renal diseases with a moderate retention of nitrogen in the blood and intensely in patients with renal disease and hyperazotemia. The intensity and duration of the increased azotemia, which follows administration of food proteins, is not proportional in all cases to the values of azotemia during fasting and before the test. The curves of induced hyperazotemia are pathologic, showing insufficiency of the kidney in some renal diseases without hyperazotemia. The test of administration of food proteins is of diagnostic and prognostic value for insufficiency of the kidney. On the basis of the changes of azotemia induced by the test, the author states that food proteins administered in the diet are of advantage in renal diseases. A diet consisting only of milk diminishes the organic resistances and causes organic dystrophies and lesions of the kidneys, which are prevented and corrected by a well directed diet containing proteins.

Clinica Medica Italiana, Turin

68: 821-900 (Dec.) 1937

*Hypotensive Action of Autohemotherapy. V. Longo.—p. 825.
Clinical and Roentgen Study of Forms of Influenza Seen in Winter of 1936-1937. R. Agnoli and A. Vallebona.—p. 867.

Hypotensive Action of Autohemotherapy.—Longo reviews the literature on autohemotherapy in cerebral hemorrhage and arterial hypertension. He concludes that autohemotherapy is of value in the treatment of cerebral hemorrhage. The technic is easy and the treatment is harmless. It gives satisfactory results in a large number of cases of cerebral hemorrhage. Autohemotherapy gives the best results in arterial hypertension. A statistical review of about 250 cases reported in the literature, which includes work carried on by the author, shows that arterial hypertension is lowered by autohemotherapy in about 91 per cent of the cases in which the treatment is resorted to. The effects of autohemotherapy are not permanent. They last for a time which varies from six months to two years or more. If hypertension reappears the treatment can be repeated, as it is harmless and controls hypertension whenever it is administered. The author discusses the mechanism of action of autohemotherapy on arterial hypertension, which is controlled by the following factors: (1) a repeated hemoclastic shock induced by the injection of the patient's own blood, (2) the development of histamine and similar substances of hypotensive action at the point at which the blood is injected and the consequent entrance of the substances in the body and (3) phenomena of immunity. The latter take place by the entrance of autoproteins in the blood which transform themselves into heteroproteins, and of hypertensive substances which transform themselves into antibodies which neutralize the hypertensive substances present in the blood of the patients.

Policlinico, Rome

45: 1-60 (Jan. 1) 1938. Medical Section

Roentgen Aspects of Muscles in Some Myopathies: Primary and Neurogenic (Charcot Marie) Types. G. Meldolesi and U. Garretto.—p. 1.
Angiotrophoneurosis: Cystic Adenoma of Thyroids with Scleroderma and Raynaud's Syndrome; Case. L. Jacchia.—p. 16.
Pseudoblock of Cerebrospinal Fluid in Sacrolumbar Malacic Acute Hematomyelitis. D. Barbieri.—p. 29.
Pluriglandular Diabetes: Cases. F. Introna.—p. 35.
*Physiopathology of Leukemic Patients: Researches on Transfusions Between Leukemic Patients. R. Gosio.—p. 42.

Physiopathology of Patients with Leukemia.—Gosio says that myelogenous and lymphatic leukemia are two opposite forms of leukemia which are caused by deficiency and excess, respectively, of unknown substances in the blood. He has done

research for ten years on the possible therapeutic effects of repeated blood transfusion between leukemic patients of the same blood group. The transfusions are given in large doses (500 cc. each) and can be repeated after ten days. Administration of crossed transfusions between leukemic patients is barred by the difficulties of reciprocal compatibility of blood groups. The author gives direct transfusion from a patient who is suffering from myeloid leukemia to one who is suffering from lymphatic leukemia, or vice versa, and immediately after that, from a normal donor to the leukemic donor. The author found that, when transfusion is done with normal blood in a patient who is suffering from lymphatic leukemia, the number of erythrocytes increases, when it is done between patients who have lymphatic leukemia, leukocytosis increases, whereas, when it is done with the blood of patients with myeloid leukemia, leukocytosis remains undisturbed. Two or four hours after transfusion, free nuclei from myelocytes and products of disintegration of myelocytes appear in the blood and slowly disappear in eighteen or twenty hours. The same results are induced by transfusion of whole blood from patients having myelogenous leukemia as by transfusion of the leukocytes deprived of plasma and suspended in a solution. The myeloid leukocytes are identified in the material which is withdrawn from the lymph nodes and the spleen, by puncture, during the first four hours which follow transfusion. Afterward, and coincidentally with the presence of free nuclei and myelocytic products in the blood, the material from the lymph nodes and spleen fails to show myelocytes or there remain but few disintegrated ones. The author states that foreign leukocytes administered by transfusion do not enter the blood. They are temporarily stored and disintegrated in the lymphopoietic structures which are concerned in the leukemic metaplasic process. The author found by experiments in vitro that the mentioned processes are not due to cytolytic properties of the blood plasma or of the blood serum. They are phases of biologic phenomena which do not take place in vitro. The phenomena are not caused by incompatibility between myelogenous and lymphatic leukocytes. Myelogenous leukocytes go selectively to the tissues which have lymphatic leukocytes. The selective localization of myelocytes in the lymphopoietic structures and the cytolysis which takes place there are reactions of defense by which the foreign leukocytes are transformed into substances which stimulate formation of new cells of the same type as those which are given by transfusion and which lack in lymphatic leukemia.

110
938

45: 53-100 (Jan. 10) 1938. Practical Section

*Bacteria in Cultures and Bactericidal Power of Gastric Juice in Gastritis and Gastroduodenitis. A. Sebastianelli.—p. 53.
*Treatment of Inguinal Hernia by Postempski's Operation. G. Cavina.—p. 57.
Spontaneous Amputation of Appendix: Case. G. B. Piana.—p. 58.

Gastric Juice in Gastritis.—Sebastianelli performed cultures and bacteriologic studies of the gastric juice of 139 patients who were suffering from gastritis of various types. The author concludes that there is no causal relation between the type of bacteria in the juice and the morphologic type of gastritis. Cultures of the juice give positive results in 72, 50 and 35 per cent, respectively, of the cases of atrophic, hypertrophic and catarrhal gastritis and in 46 per cent of the cases of gastroduodenitis. The bactericidal power of the gastric juice is altered in 91 per cent of the cases of atrophic gastritis, 72 per cent of those of hypertrophic and catarrhal gastritis and 75 per cent of the cases of gastroduodenitis. The alterations of the bactericidal power of the gastric juice take place much earlier than the appearance of bacteria in the juice. The author states that the determination of the bactericidal power of the gastric juice is of value for an early diagnosis of gastritis and that the test is more reliable than the results of the cultural examination of the gastric juice.

Treatment of Inguinal Hernia.—Cavina says that for the plastic reconstruction of the inguinal canal in the treatment of inguinal hernia he resorts to a modification of Postempski's operation, which in turn is a modification of Bassini's. The technic is as follows: The muscular layer, with or without the fascia of the transversalis muscle, is sutured by three or four catgut stitches to Poupart's ligament. The aponeurosis of the external oblique muscle is then sutured, also with catgut, following a direction from the pubic bone toward the anterior superior spine of the ilium. The spermatic cord is made to emerge through the aponeurosis of the external oblique muscle at the highest point near the internal inguinal ring. The sutures at the point of emergence of the spermatic cord are done with silk of an average thickness. The spermatic cord lies bent on the pad and is protected from proximity to the external part of the body by placing in front of it the cellular fascia and the subcutaneous tissue. Recurrences of herniation, especially at the upper region of the incision, are prevented by following the author's technic. The author obtained satisfactory results from the operation in more than 1,000 cases of inguinal hernia. The operation is indicated in inguinal laparocele, direct and recurrent inguinal hernia, external oblique hernia and also when the spermatic cord is large and may be injured by the scars left by following Bassini's technic.

Semana Médica, Buenos Aires

45: 57-112 (Jan. 13) 1938. Partial Index

Treatment of Supra-Acromial Luxation of Clavicle. T. Gioia.—p. 57.
Extramembranous Pregnancy: Cases. M. V. Falsia and A. Falsia.—p. 61.
Spontaneous Choleperitoneum, Also Called Biliary Peritonitis and Filtrating Cholecystitis: Cases. A. Pierini.—p. 65.
Acute Hemopathy After Tonsillectomy. L. Sánchez Moreno.—p. 84.
*Gastroduodenal Perforation: Eighty-Five Cases. G. Boneo and E. A. Ramírez.—p. 104.

Gastroduodenal Perforation.—Boneo and Ramírez's study of perforation of gastroduodenal ulcers is based on observations made in eighty-five cases during the last five years in the Pirovano Hospital. All patients but one were men. The authors conclude that perforation of gastroduodenal ulcers take place almost exclusively in men ranging in age from 30 to 40 years, after which it is rare. Perforation occurs more frequently in gastric than in duodenal ulcers and is most frequent in autumn and winter. In the group of patients seen by the authors, perforation took place within the third and sixth hours after ingestion of food or fluids. There was a history of gastric or duodenal disturbances in 94 per cent of the cases. The treatment is surgical and urgent. It consists in simple suture of the perforation, with omentoplasty and without drainage, in patients in good general condition, with short hours of evolution of perforation and who do not show symptoms of peritoneal contamination. Otherwise a local or suprapubic drainage is left. Mortality increases in relation to the age of the patient and to the hours elapsed between the time of the perforation and the surgical intervention.

Archiv für Dermatologie und Syphilis, Berlin

176: 201-346 (Dec. 8) 1937. Partial Index

Aspects of Fordyce's Condition and Its Significance for Clarification of Problem of Localization of Cutaneous Disorders of Oral Cavity. K. Halter.—p. 201.
Clinical Aspects and Histology of Chronic Ulcerous Pyodermia. P. Balog.—p. 228.
*Action of Arsenobenzol Preparations on Fetus. L. Vamos and A. Böhm.—p. 245.
Diffuse Sclerodermia Complicated by Leukemia and Improved by Parathyroidectomy. T. Kusunoki and S. Kuwabara.—p. 256.
*Action of Sodium Borate on Important Fungi. A. Dósa.—p. 261.
*Generalized Herpes Zoster in Leukemia. J. Ferreira Marques.—p. 295.
Ecthyma Contagiosum of Sheep and Its Transmissibility to Human Subjects. T. Oppermann and G. Stümpke.—p. 337.

Action of Arsphenamine Preparations on Fetus.—Vamos and Böhm studied the action of arsphenamine on the fetus following administration to the mother. They conclude that arsphenamine can be demonstrated in the organs of the pregnant organism, in the decidual vessels and in the intervillous spaces, but not in the chorion or in the fetal organs. Since the independent defense of the fetus against a syphilitic infection is inadequate as the result of the impermeability of the chorion, it is important that energetic treatment is begun before or at the beginning of the pregnancy.

Action of Sodium Borate on Fungi.—Dósa's clinical observations convinced him that borax is of therapeutic value not only in thrush mycosis of the skin but also in other cutaneous mycoses. The author experimented with the alkalization

of fungus cultures. Tests were made on cultures of Kaufmann-Wolf's epidermophyton, of saccharomyces and of other fungi. Borax in different concentrations was added to the Sabouraud maltose-agar nutrient mediums that contained the fungi. To determine whether alkalization was the decisive factor, experiments were made also with dehydrated sodium carbonate, sodium carbonate and boric acid. It was found that borax exerts not merely an alkalizing but rather a specific action. Although boric acid proved more effective than borax in the culture mediums, the author prefers borax for the treatment, since boric acid is not always harmless for the skin, whereas borax is free from injurious effects, even if used in high concentrations.

Generalized Herpes Zoster in Leukemia.—Ferreira Marques differentiates between idiopathic or primary and symptomatic or secondary herpes zoster. He gives attention to the second type, particularly that which develops in chronic leukemia. He reports the history of a man, aged 76, who had complained of pains in the left side of the neck and head. Later, herpes zoster developed on the same site and gradually involved the whole trunk. A week later facial paralysis could be observed and the author assumes that it was connected with the herpes zoster. Examination disclosed enlargement of the liver and spleen and the presence of 140,000 leukocytes, of which 92 per cent were lymphocytes. The author tabulates the formerly reported cases of herpes zoster and leukemia. Of forty-two cases of herpes zoster, thirty-four were associated with lymphatic leukemia and only three with myeloid leukemia. The herpes zoster develops usually between the second and third year of the leukemia. Herpes zoster is most frequent in patients between the ages of 50 and 60. The majority of patients are men. Paralysis was observed in two cases of facial paralysis and two of paralysis of the extremities. From a study of the literature and observations on the reported case, he concludes that there is nothing known to contradict the theory that the herpes zoster in leukemia is caused by a virus.

Klinische Wochenschrift, Berlin

16: 1777-1808 (Dec. 18) 1937. Partial Index

Acute Porphyria and Hemoglobinuria. W. von Drigalski.—p. 1779.
Determination of Conductors and Distribution of Blood Groups in Hemophilia. S. Löfgren.—p. 1782.
Experimental Contribution to Hypophysial Manifestations of Abolished Function by Hormones of Anterior Lobe of Hypophysis. H. E. Never. —p. 1785.
Relations Between Sympathetic and Trophic Innervation of Fat Tissue. Ken Kuré, Toshio Oi and Shigeo Okinaka.—p. 1789.
*Vitamin C Elimination in Urine and Vitamin C Content of Cerebrospinal Fluid in Nervous Disorders. Olga Altmann and Helene Goldhammer.—p. 1793.
*Chemical Composition of Normal and Pathologic Bile of Liver and Gallbladder. E. Prado Tagle and G. Kurth.—p. 1795.
Recognition and Evaluation of Chronic Tonsillitis in Rheumatic Diseases. F. Knüchel.—p. 1797.

Vitamin C in Nervous Disorders.—Altmann and Goldhammer made protracted tolerance tests with vitamin C in twelve patients with nervous disorders. Their aim was to detect a possible relationship between a diffuse, anatomically demonstrable impairment of the central nervous system and a disturbance in the vitamin economy. The results of the tests gave no indications of such a relationship. Thus the authors were unable to corroborate Bersot's opinion, according to which a retarded or lacking elimination of vitamin C, after a prolonged tolerance test, is the manifestation of a metabolic disturbance in the brain. However, the results did indicate that age plays some part in the retarded elimination. The manner of elimination of the vitamin during the tolerance test was not dependent on the values that were observed before the tolerance test was begun. After the tolerance test was completed, the increased elimination ceased suddenly. The authors also determined the vitamin C content of the cerebrospinal fluid of twenty-four patients with various nervous and mental disturbances. In comparing the results with the normal averages determined by Plaut and Bülow in persons without cerebral disturbances, they found that the vitamin C content of the cerebrospinal fluid was reduced in such disorders as epilepsy, tabes dorsalis, dementia paralytica, cerebral arteriosclerosis, latent syphilis and enterococcic myelitis. The greatest deficit was found in a case of herpes zoster.

Chemical Composition of Normal and Pathologic Bile.—Prado Tagle and Kurth investigated the chemical composition of the normal bile of the liver and of the normal and pathologic bile of the gallbladder. On the basis of their observations they reach the conclusion that impairment of the gallbladder is characterized by an almost 100 per cent increase in the mucin content of the bile. There is also a considerable increase in bile salts. The dry residue is low, which indicates a decrease in the substances that are dissolved in bile and thus also a reduction in the concentration capacity of the gallbladder. The bilirubin and cholesterol contents are normal. These observations suggest that, in case of impairment of the gallbladder, that chemical function of the liver which concerns the formation of bile acids is impaired. It seems to be reduced. In contradistinction to this, the capacity for the elimination of cholesterol and bilirubin is intact. The content in these "waste substances" is frequently even increased. This disturbance in the chemical function of the liver is probably a contributing factor in the development of gallstones, for bile salts facilitate the solubility of cholesterol and bilirubin. The lack of these substances favors the precipitation of the lipoids and of the biliary pigments. These factors throw light on the pathogenesis of gallstones, particularly if the increase in mucin is likewise taken into account. The latter interferes with the evacuation of the gallbladder, because it increases the viscosity. This in turn produces biliary stasis and favors the growth of microbes in the infected gallbladder. Mucin promotes the accumulation of sediments. This is important for the formation of the nucleus of gallstones. The hypersaturation phenomena of cholesterol and bilirubin promote the growth of gallstones around this nucleus.

Monatsschrift für Kinderheilkunde, Berlin

71: 305-460 (Dec. 13) 1937

Contribution to Problem of Renal Infantilism. W. Malz.—p. 305.
Lymphadenitis and Nephritis in Scarlet Fever. J. Wolff.—p. 310.
Solitary Tubercle in Pons Varolii in Nursling, Aged 8 Months. H. Peter. —p. 316.
*Tetany During Early Infancy. H. Baar.—p. 321.
*Syndrome of Waterhouse-Friderichsen. A. Kamber.—p. 351.
Influence of Phosphoric Acid on Mineral Metabolism of Children. E. Bauer.—p. 374.
Investigations on Bone Marrow in Living Nurslings. G. Joppich and P. Liessens.—p. 382.

Tetany During Early Infancy.—Reviewing the literature on tetany of early infancy, Baar points out that, whereas some authorities deny the appearance of this disorder during the first months of life, others consider it a rather frequent occurrence. It is difficult to diagnose tetany during early infancy because tetany of the new-born, brain lesions caused by the trauma of birth and septic encephalitis of the new-born may cause the same symptoms. Even the symptoms of latent tetany, particularly those of mechanical hyperirritability, may fail. The only sign that has pathognomonic value is that of Thiemich-Mann (cathodic hyperirritability), and even this is of use only when it is positive. If it is absent, it is necessary to make a chemical analysis of the blood or to analyze the acid-base equilibrium in the urine. The author reports two cases of tetany that occurred during early infancy. The first case proved to be a tetany caused by an absolute phosphate stasis, which, in turn, was presumably caused by a disturbance in the central regulation. In the second nursling there existed a hematogenic alkalosis caused by hyperthyroidism. The author emphasizes that among the cases of tetany of early childhood it is necessary to differentiate the early form of rachitogenic tetany and the tetany of early infancy in the strict sense of the term. The pathogenesis of the latter is not uniform. Among the cases described in the literature, three different forms can be differentiated, and on the basis of the described observations two forms should be added to these; namely, the tetany caused by absolute phosphate stasis and the thyrogenic tetany.

Syndrome of Waterhouse-Friderichsen.—Kamber reviews the earlier literature on the syndrome of Waterhouse-Friderichsen and then describes a case observed at the children's hospital in Bern. Of the sixty-two cases reported so far, forty concerned children less than 2 years of age. How-

V 1
193

ever, the literature reports also twelve cases occurring between the ages of 18 and 24 years and two in middle age. In the majority of cases there is no prodromal stage; the syndrome develops suddenly in children who have apparently been in complete health. The child wakes up with a sudden cry and soon there is vomiting. The face becomes pale and then cyanotic. Consciousness is more or less impaired. The temperature may at first be only slightly above normal but it increases rapidly. The respiration is accelerated and accompanied by sounds. Occasionally tonoclonic twitching is observable on the face and arms. These spasms may last for several minutes. In the reported case they recurred until the fatal outcome. Following the period of jactitation, the child becomes quiet and apathic; the facial expression is anxious; the eyes are dull and half open; the temperature rises to extreme heights; the pulse is extremely rapid and soft; the blood pressure is so low that it can hardly be measured; the respiration is greatly accelerated, superficial and of the pneumonic type; movements of the ala nasi are often observable. The abdomen is usually somewhat inflated but soft and not sensitive. Aside from loss of consciousness and the tonoclonic convulsions, there are hardly any nervous symptoms. The cerebrospinal fluid is usually normal. Several hours before death, petechial hemorrhages appear and these are usually followed by a generalized purpura. The respiration becomes of the Cheyne-Stokes type. Nystagmus, strabismus and convulsions may precede death. The disease takes its course in from six to twenty-four hours. In adults the clinical course is similar to that in children, except that meningitic symptoms are more frequent. The cutaneous symptoms, which may suggest exanthematic infectious diseases, are important for the diagnosis as is also the cyanotic coloration of the skin, which involves especially the face, trunk and lower extremities. The gray and violet-blue spots give the body a marmorated appearance. Moreover, the extremities may become cold while the trunk is still hot. Discussing the pathologic anatomy of the Waterhouse-Friderichsen syndrome, the author stresses the changes in the adrenals. These organs are usually slightly enlarged and show a purple-red to brownish black discoloration, the result of the profuse blood supply. They may be veritable sacs of blood with only slight remnants of normal glandular tissue. Microscopic examination reveals hemorrhagic infarction of the cortex and medulla. Microscopic examination of the cutaneous petechiae discloses dilatation of the vessels and diapedesis into the tissues. Necropsy reveals that mucous membranes as well as the internal organs may have petechiae or hemorrhages. The central nervous system often shows hyperemia. Etiologically, hyperacute infection has been suggested and there is evidence that meningococci play an important part. Constitutional factors are apparently of importance. Status thymicolymphaticus is mentioned in many reports or there may be a hyperplasia of the lymphatic system. In view of the unfavorable prognosis, therapy is of little avail. However, in addition to combating the circulatory collapse, specific serotherapy and blood transfusions could be tried and, to counteract the adrenal insufficiency, cortical extracts, epinephrine and dextrose should be given.

110
938

Wiener klinische Wochenschrift, Vienna

50: 1763-1794 (Dec. 31) 1937

*Basal Metabolism and Hyperthyroidism. J. Bauer.—p. 1763.
Crisis of Pathophysiology. A. Greil.—p. 1766.
Cytologic Examination of Palatine Tonsils and Its Clinical Significance in Leukemia. H. Brunner and J. Schnierer.—p. 1772.
Nature and Therapy of Spondylarthritis. A. Lux.—p. 1774.
Progress in Therapy of Female Gonorrhea. S. Wolfram.—p. 1776.

Basal Metabolism and Hyperthyroidism.—Bauer points out that it has been assumed that the elevation of the basal metabolic rate, which is produced by an increase in the organic processes of combustion, is the result of some catalytic stimulation of the cellular oxidation by thyroxine. Eppinger, however, suggested an entirely new hypothesis regarding the cause of the increase in the basal metabolism during hyperthyroidism. In the musculature of patients with hyperthyroidism and in that of animals poisoned with thyroxine Eppinger discovered a thickening of the capillary walls and other changes, which he interpreted as a sign of serous inflammation. He reasoned that these changes inhibit the passage of the oxygen from the blood into the tissues; that is, that they result in a deficient oxygen supply of the musculature, which in turn would impair the resynthesis of the lactic acid that is produced by the contraction. Since larger quantities of oxygen are required to remove the lactic acid, the oxygen debt is increased above the normal. Bauer criticizes Eppinger's theory. He shows that the increase in basal metabolism in patients with hyperthyroidism is caused by a direct action of the thyroid hormone on the cells, the anoxybiotic cleavage processes of which are augmented and the oxygen consumption of which is consequently increased. Disturbances in the carbohydrate content of the muscle cause disturbances in the muscular activity and this explains the disappearance of glycogen, the accumulation of lactic acid and the greater oxygen debt after muscular work. The organism compensates for the increased oxygen requirements by greater peripheral blood perfusion. Increased minute volume, greater circulatory velocity and other factors make possible an adequate oxygen supply for the tissues. As a result of these processes, the tisstues can be supplied with more oxygen without there being an increased utilization and a greater arteriovenous difference in the oxygen. The author concludes that an increasing effect on the metabolism must be regarded as the specific action of the thyroid hormone and that Eppinger's theory must be rejected.

Vrachebnoe Delo, Kharkov

20: 337-416 (No. 5) 1937. Partial Index

Lysate Therapy. S. G. Genes.—p. 337.
Lysate Therapy in Cardiovascular Diseases. E. A. Chernikov, E. Ya. Sterkin, S. Kh. Malyar and F. M. Vengerova.—p. 343.
Lysate Therapy of Gastric and Duodenal Ulcers. N. M. Dukhin.—p. 349.
*Lysate Therapy of Muscular Dystrophy. D. M. Zalkan and R. M. Kurzon.—p. 353.
*Lysate Therapy of Chronic Polyarthritis. P. R. Normark, P. F. Frolov, Z. S. Edel, I. M. Markus, I. S. Leonov, M. O. Pasko and N. I. Sokolovskaia.—p. 367.

Lysate Therapy of Muscular Dystrophies.—Zalkan and Kurzon report the effect of lysate therapy in fourteen cases of chronic progressive muscular atrophy. Myomyelohepato-ovarian or testicular (depending on sex) combinations of lysates were used together with administration of strychnine after the method of Bier and Gehrke. Each patient was given four courses of treatment consisting of twenty injections each. The interval between individual injections amounted to two weeks. A definite subjective and objective improvement was noted in ten. The improvement was noted in the course of the treatment or, more frequently, at the end of or sometime after the treatment. The patients developed a sense of well being, an increase in energy and working capacity and a diminution of fatigue. The gait improved, the patients did not fall as frequently and were able to descend and to climb stairs with greater ease. There was an increase in the muscular power and an increase in the circumference of the extremities. In some of the cases a lowering of the threshold of the electrical excitability was noted. The improvement lasted from six months to two years. The authors do not claim for histolysates the ability to effect cure in cases of progressive muscular atrophy. However, in view of the utter helplessness of these patients, the improvement they have noted in their cases is significant. The mode of action of lysate therapy in these cases is not understood.

Lysate Therapy of Chronic Polyarthritis.—Normark and his associates report the results obtained with chondrolysates, arthrolysates alone and in combination with galvanotherapy in ninety-eight patients, forty-eight of whom suffered from chronic rheumatic polyarthritis and fifty from chronic infectious arthritis. The injection of lysates alone or in combination with galvanotherapy produced both focal and general reaction of the kind observed in all methods of nonspecific protein therapy. As a result of a course of graded doses of intracutaneous injections of lysates alone for a period of from thirty to thirty-five days in twenty-four cases of chronic and subacute infectious polyarthritis, the authors noted in twenty-two improvement of the local lesions and of the general state of health. The combination of the lysate therapy with galvanotherapy gave an even better result. They have noted a

considerable improvement in the majority of the patients, amounting in some cases to a clinical cure. They have demonstrated, in patients showing improvement in symptoms, a simultaneous return to the normal on the part of the vegetative nervous system, of the reflexes, of the potassium-calcium index and of the leukocytic formula, as well as an increase in the quantity of hemoglobin, diminution of the leukocytosis and of the number of reticulocytes, and a retardation of the sedimentation speed. The positive results persisted in about two thirds of the cases for one year. Recurrences were observed most frequently in the cases of rheumatic polyarthritis.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

81: 6099-6162 (Dec. 25) 1937

General Cutaneous Pigmentation in Internal Diseases. P. Formijne.—p. 6100.
*Tests in Connection with Several Unsolved Problems Concerning Epidemiology of Weil's Disease. P. H. Van Thiel.—p. 6106.
Tubal Pregnancy. A. J. M. Duyzings.—p. 6128.
Rare Neurologic Disturbances During Pregnancy and After Delivery. G. Stoel.—p. 6136.

Epidemiology of Weil's Disease.—Van Thiel reports investigations on some unsolved problems in connection with the epidemiology of Weil's disease. The first question he takes up is how long Leptospira icterohaemorrhagiae survives in free surface water. His investigations revealed that during the swimming season it survives for at least twenty-two days and that its virulence remains intact during this entire period. After six days these pathologic leptospirae have a tendency to go to deeper levels. Near mud or in water that is contaminated with urine, the organism can keep alive without loss of virulence for at least five or seven days. In waters that are used for bathing and swimming, the leptospirae may be brought from the deeper to the higher levels and may infect the swimmers. Bathing establishments situated on open waters and from which rats are kept by means of wooden partitions are not sufficiently safe, because the wooden partition will not prevent the entrance into the swimming establishment of the leptospirae excreted by rats outside the partition. Guinea pigs can be infected with the avirulent as well as with the virulent strains of Leptospira icterohaemorrhagiae. Moreover, the animal organism can be invaded by the saprophytic Leptospira pseudoicterogenes. Although epidemiologic data do not indicate that human beings become infected with Leptospira canicola during bathing, this is nevertheless possible under certain conditions. In connection with experiments on guinea pigs, it is assumed that the infection of human subjects with a few avirulent organisms of Leptospira icterohaemorrhagiae protects against a mild infection with virulent leptospirae of the same species only in case of a response of the organism to this immunizing infection, which is indicated by the development of agglutinins or lysins. Experiments on guinea pigs give promise that immunization of human subjects to a degree that provokes only a low titer in the serum will generally provide protection against Weil's disease.

Finska Läkaresällskapets Handlingar, Helsingfors

80: 785-849 (Oct.) 1937

*Diagnosis and Treatment of Bronchiectatic Disorder. J. Holst.—p. 794.
Roentgen Treatment of Thyrotoxic Edema of Temples. J. Wahlberg.—p. 813.
Method for Otologic Diagnosis of Cerebrospinal Fluid. H. Björk.—p. 818.

Treatment of Bronchiectatic Disorder.—Holst states that the bronchiectasis is the product of two factors, distended bronchi and infection. Diagnosis is verified roentgenologically by bronchography. Complicating pneumonia, pulmonary abscess, empyema or metastatic abscess, often occurring surprisingly late, is the frequent cause of death. Treatment is surgical (lobectomy). Patients having bronchiectatic cavities expectorate massive quantities in the first few hours after rising. Possible bronchiectasis should be considered in suspected pulmonary tuberculosis when tubercle bacilli cannot be demonstrated in the sputum. In cases complicated by pneumonia, abscess or empyema, diagnosis may be especially difficult. Bronchiectasis may be latent for years. The technic of lobectomy is not yet fully solved. Most bronchiectatic disorders alternate between periods with more scanty and with more profuse expectoration; operation should be timed for the drier period. Temporary pneumothorax was done four or five days before operation. He stresses full narcosis before the opening of the pleura and tries by large morphine-scopolamine doses to suppress the cough reflex before the beginning of narcosis. His present view is that lobectomy is not indicated in clinically latent cases or in those showing only periodic symptoms, with moderate amount of expectoration and nonfetid expectoration. It is indicated in patients with more than 40 or 50 Gm. of expectoration daily or with fetid expectoration. The nineteen cases of primary bronchiectasis reported illustrate the tendency of the disorder to be localized in one of the lower lobes. In three cases there were large bronchiectatic cavities. In nine cases the diagnosis had been pulmonary tuberculosis. In half the cases the symptoms began in childhood, in one third in early childhood and in one instance at the age of 40. Ten lobectomies were done, two in one patient who died from empyema after the second intervention. Most of the patients had a rather marked postoperative reaction. Seven are without symptoms.

Hospitalstidende, Copenhagen

80: 1333-1356 (Dec. 21) 1937

*Microscopic Investigations in Some Cases of Fibro-Adenomatosis of Breast with Especial Regard to Effect of Treatment with Estrogen. F. Sørensen.—p. 1333.

Estrogen in Treatment of Fibro-Adenomatosis.—Sørensen made seventeen biopsies in sixteen patients, ranging in age from 16 to 46, with fibro-adenomatosis of the breast. In the eight untreated patients he found the hyperplasia of the intralobular connective tissue considerably more intense than in the nine who were treated with estrogen. In the patients treated with estrogen there was a remarkable succulence resembling normal menstrual edematization in the intralobular connective tissue. Cytologic examinations of the glandular epithelium in the premenstrual, menstrual and postmenstrual stages of the two groups showed enlargement of the Golgi substance and closer arrangement of the mitochondria. The same relation was seen in two patients effectively treated with estrogen and examined in the interval stage. In four patients of seven examined before treatment the excretion in the urine of gonadotropic substance, estrogen or both was reduced.

Hygiea, Stockholm

99: 897-928 (Dec. 31) 1937

*White Blood Corpuscle Picture in Uncomplicated Pleurisy in Pneumothorax and in Pleurisy in Pneumothorax with Simultaneously Occurring Aggravation of Parenchyma Process. H. Hallander.—p. 904.
Common Descent of Eighteen Physicians. S. Tingvall.—p. 910.

White Corpuscles in Pleurisy.—Hallander says that, at the start of the pleurisy in his twenty-seven cases, no difference was demonstrable between the degree of shifting to the left in the sixteen uncomplicated cases and the eleven with aggravation or spread of the pulmonary process, but that in the latter the shifting to the left due to the aggravation of the parenchyma process continued after the pleurisy began to recede. When the pleurisy set in slowly and without particular reaction in shifting to the left, there appeared at the beginning of the aggravation of the pulmonary process an increased shifting to the left which did not correspond to the exacerbation of the pleurisy and which increased parallel with the progression of the process. The difference between the blood picture in the uncomplicated cases and in those with aggravation of the parenchyma process was so marked that, after the general reaction accompanying the onset of the pleurisy subsided, examination of the white blood corpuscle picture afforded an indication of the cases in which an aggravation of the pulmonary process was to be expected. In five of the eleven cases the continued shifting to the left after both temperature and sedimentation values had become normal was the only sign that the aggravation still persisted; in two of the cases the aggravation was not roentgenologically demonstrable until after the temperature and sedimentation values had fallen.

V 11
1938